Volume XX Number 3

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DISEASES OF THE NERVOUS SYSTEM

A Practical Journal on Psychiatry and Neurology

MARCH
1959

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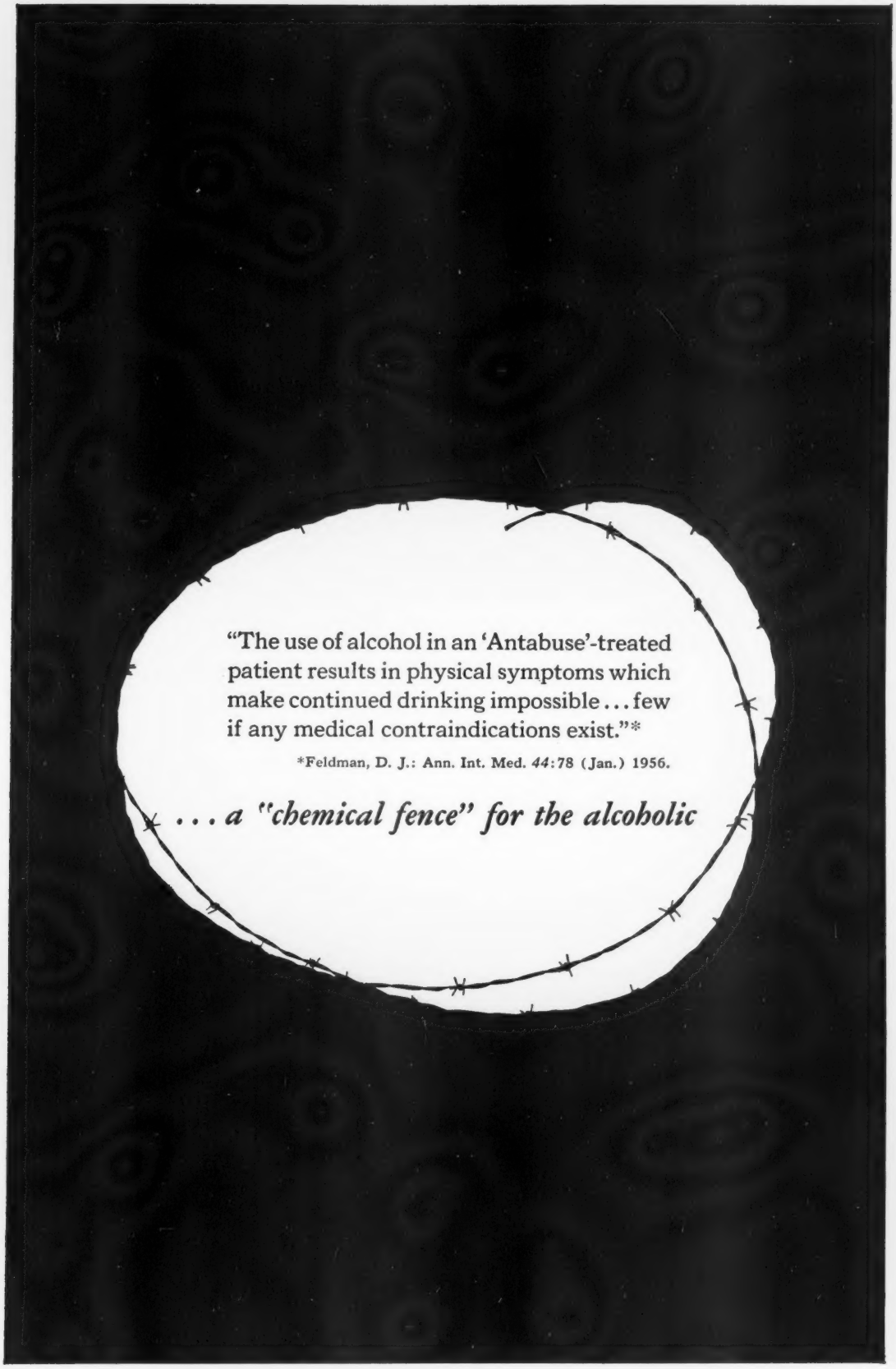
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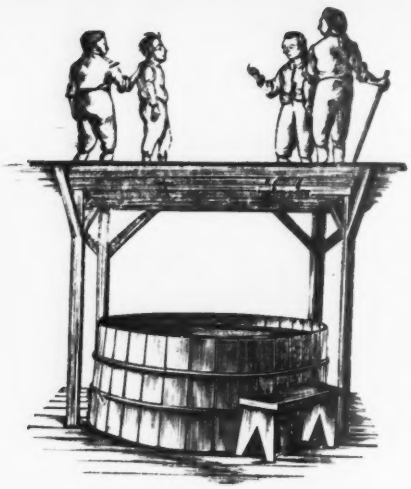

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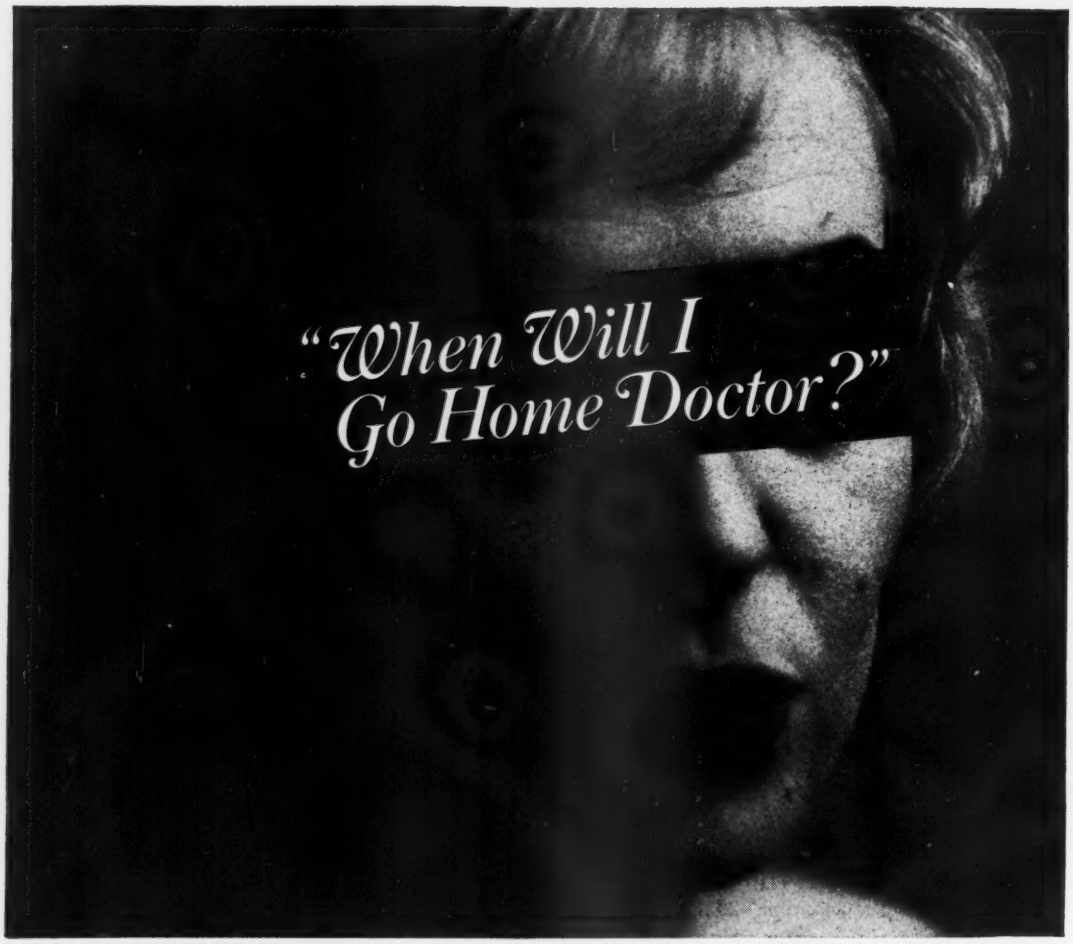

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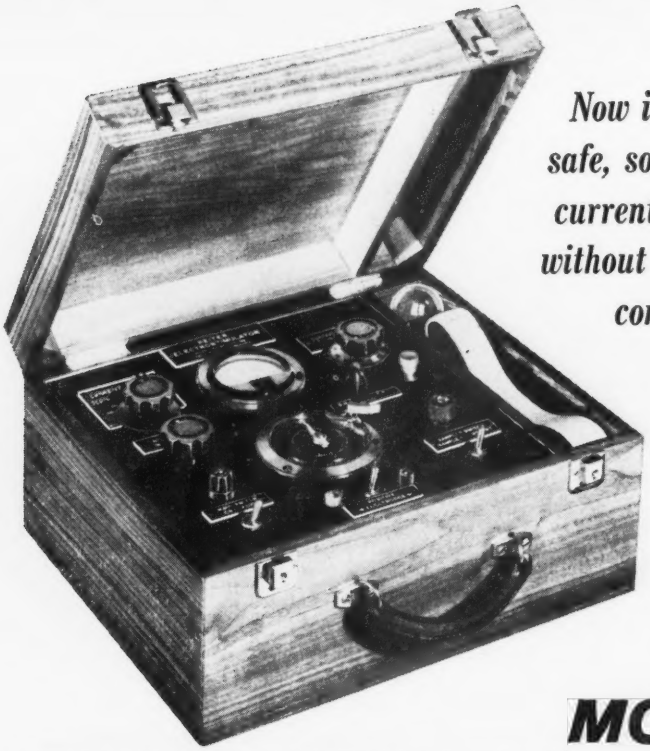

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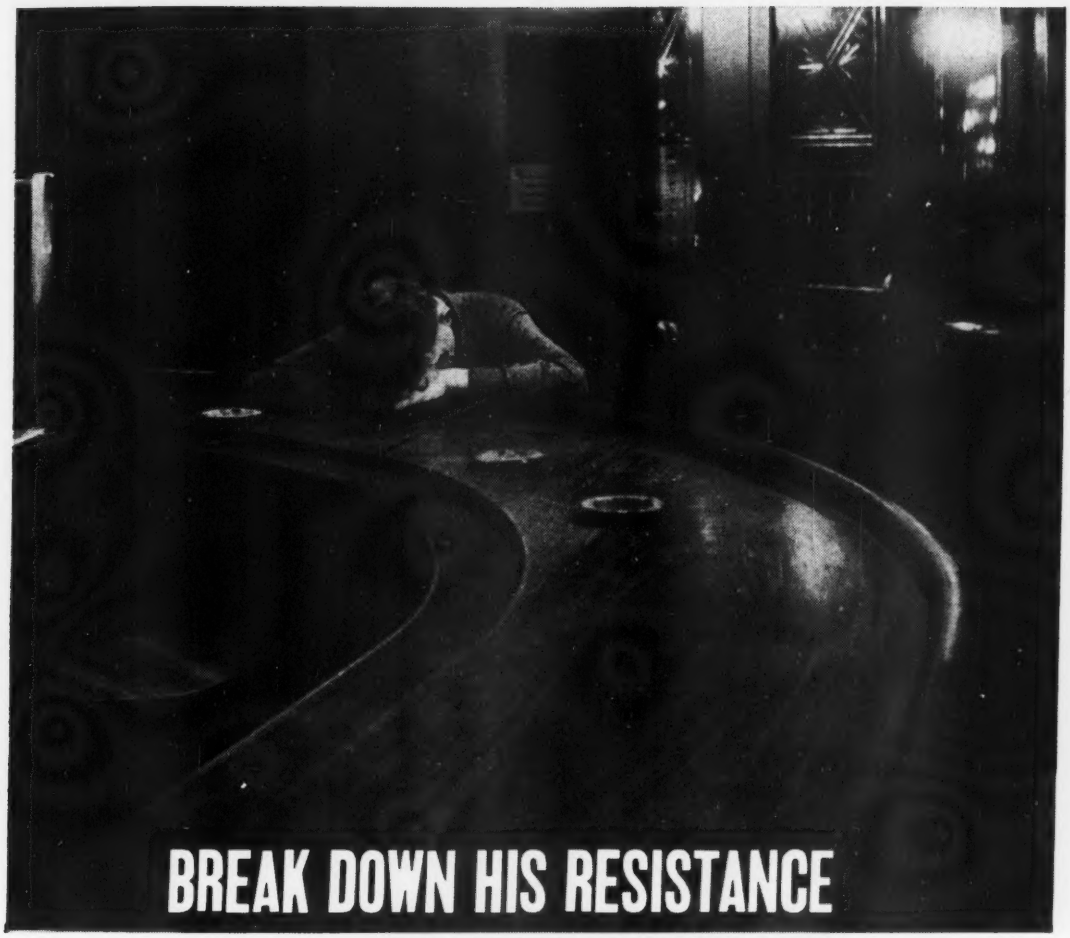

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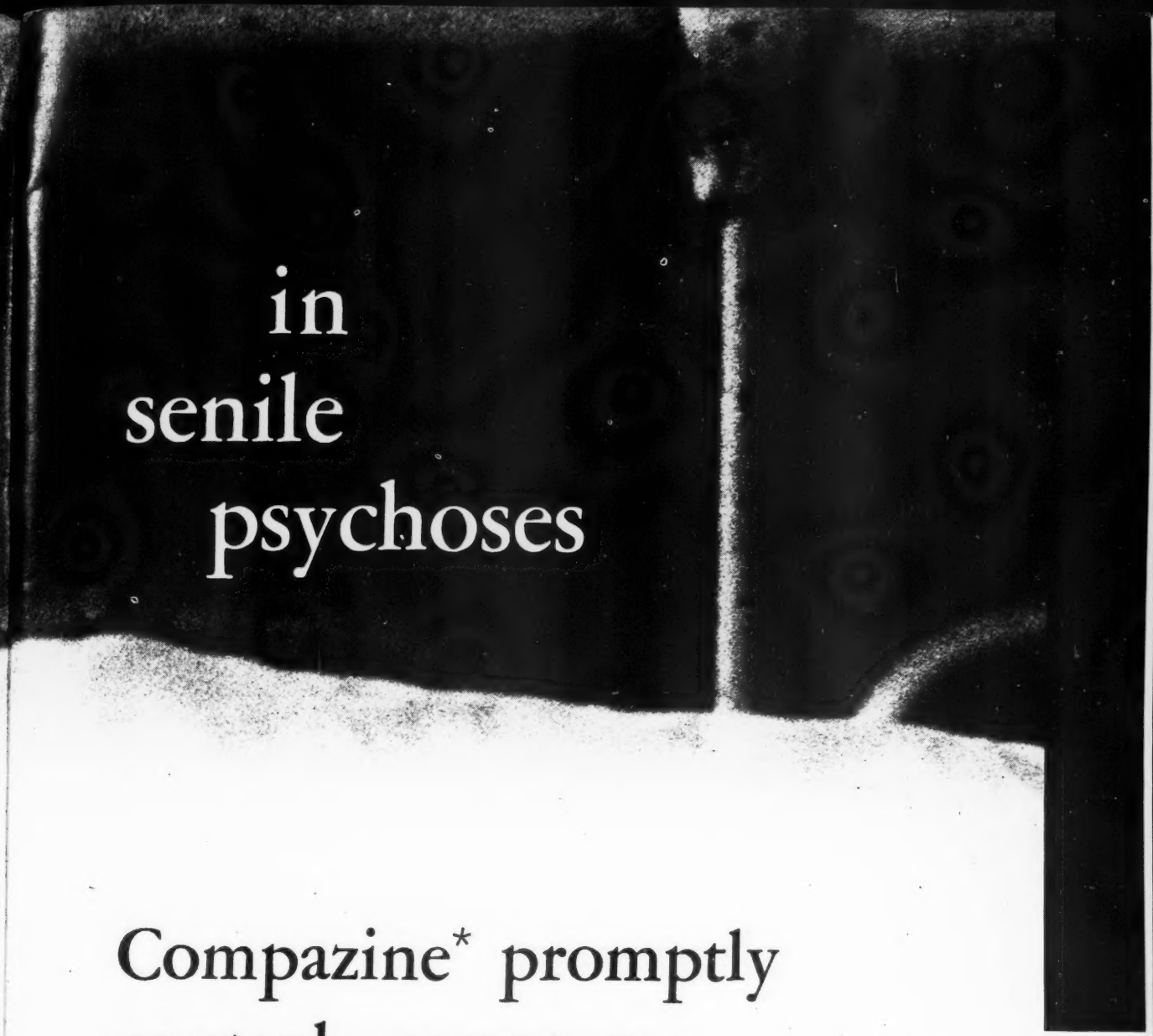

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*Vorbusch, H.: Mepazine [Pacatal] in the Treatment of Psychiatric Disorders with One Year Follow-up, in press.

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Gunther's Accommodation Index

JORGE WEIBEL, M.D.

In the diagnosis of several neuromuscular diseases the theoretical knowledge of electrophysiology has been employed in order to find a useful procedure to complement the clinical study. Several instruments which generate galvanic rectangular pulsatile, alternating and condenser discharge currents have been used. By these means the technique for registering nerve and muscle potentials have been improved. (Fig. 1.)

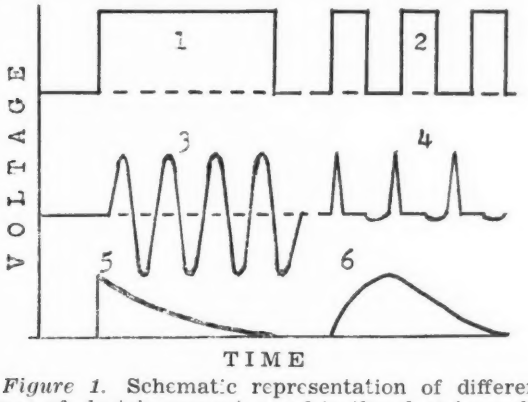

Figure 1. Schematic representation of different types of electric currents used in the electric exploration of the nerve and muscle. 1. Galvanic; 2. Rectangular pulsatile; 3. Alternating; 4. Faradic; 5. Condenser discharge; 6. Exponential.

Since 1948 experiments have been conducted in order to evaluate the practical importance of the Gunther's Accommodation Index (GAI)[1] in both the diagnosis and prognosis of neuromuscular diseases. This procedure is based on the nervous accommodation phenomenon. The concept of nervous accommodation, however, is not new. It was known long before the excitability in function of time (useful time and chronaxie) was discovered. Du Bois Raymond (1849), among the first electrophysiologists, realized that an electric current with slow ascending or descending speed required higher voltage to excite a nerve than the galvanic current which reaches its maximum value and descends from it in a vertical manner. Thus, if the stimulating current ascends slowly to its maximum value the threshold of excitability also increases gradually, so that the voltage necessary to obtain a response is higher than its threshold with galvanic current. Nerst termed this phenomenon of unknown nature, "accommodation."

In 1941, Gunther[2] working with exponential currents (currents with slow ascending and descending speed) found a relationship between the constant of time and the speed with which the accommodation is accomplished. Therefore, when the chronaxie is short the accommodation index is high, as is the case with the isolated nerve of a normal neuromuscular preparation. On the other hand, the heart muscle, which has a long chronaxie, has a low accommodation index. In his observations he also found a remarkable diminution of the accommodation in cases with neuromuscular degeneration of peripheral type and this coincided with a considerable increase in the chronaxie and a slow muscular contraction in response to the electrical stimuli. According to his experiments, he advised the use of the exploration of the accommodation index as an electrodiagnostic procedure in the neuromuscular diseases.

In 1948, Gunther and Weibel[3] did a statistical study of the accommodation index in normal individuals. The author[4,5] studied the modifications of the nervous accommodation in wallerian degeneration and the influence of ischemia on the threshold and the nervous accommodation in man. These findings suggested a practical application of the accommodation index in electrodiagnosis and prognosis of the neuromuscular diseases.

From Department of Neurology, Baylor University College of Medicine, Houston, Texas. Author on leave of absence from University of Concepcion, Conception, Chile.

Method

In this work an instrument designed by Gunther and Concha (Institute of Physiology of the University of Concepcion, Chile) was used. The instrument generates two types of exponential ascension which are designated E_1 and E_2. The E_1 reaches its maximum voltage at 20 milliseconds, while E_2 obtains its highest voltage at 50 milliseconds. The stimulator is calibrated according to the effective voltage of the charge condenser, which discharges through a net of condensers of specific capacity and generates the two types of exponential current mentioned above. This calibration permitted the determination of the relative threshold of the excitable tissue to two exponential currents which reach their highest voltage at different times. In order to determine the thresholds, a small electrode (cathode) 1 cm. in diameter is placed on the skin overlying the muscles or nerve to be stimulated. The large electrode (anode) is represented by a metal cylinder, 8 cm. in length and 2.5 cm. in diameter, which the patient holds in one of his hands. The contact between the metal electrodes and the skin is obtained by a piece of cloth impregnated in saline solution. The threshold (minimum muscular contraction) to E_1 is first determined and afterwards the threshold with E_2. It is important to take care in obtaining the same magnitude of muscular response repeatedly. To be sure, it is necessary to recheck the results three or four times. Once the threshold values to E_1 and E_2 have been obtained, the voltage of E_2 is divided by the voltage of E_1. The E_2/E_1 coefficient is an index of the accommodation of the nerve or muscle studied. If E_2/E_1 is 1.0 this means that accommodation is practically absent, a finding observed in nerve-muscle preparation with complete wallerian degeneration. Values of E_2/E_1 less than 1.25 and higher than 1.0 have been observed in partial nerve degeneration. The neuromuscular system under normal conditions consistently shows E_2/E_1 values higher than 1.25.

Material

In this report only the electrodiagnostic and prognostic values of the Gunther's Accommodation Index (GAI) are described in cases of paralysis of the peripheral nerves. Some studies in other neuromuscular disorders have already been published.[6] The number of cases are represented in Table I.

TABLE I—*Distribution of 191 Cases of Peripheral Nerve Paralysis and Clinical Result.*

	Recovered	Not Recovered	Total
Facial	106	15	121
Radial	42	2	44
Peroneal	7	3	10
Sciatic	–	2	2
Ulnar	5	2	7
Median	3	–	3
Brachial Plexus	2	2	4
Total	165	26	191

Results and Discussion

In order to provide an understanding of the evolution of the GAI in the course of paralysis of peripheral nerves the results in three groups of patients are reported. These groups are separated on the basis of exploration of the accommodation index as determined directly on the muscles, with or without loss of excitability or conductivity through the nerve. In each group a case with paralysis of the facial and/or radial nerves will be described in detail. These are representative cases for each group.

Group A. These patients showed complete reaction of degeneration with diminution of the muscular GAI and loss of excitability through the nerve. (Paralysis with complete reaction of degeneration.) This group is subdivided into two subgroups.

Subgroup A-1. The patients included in this subgroup had a favorable course with complete recovery of voluntary movement (paralysis with complete reaction of degeneration recovered). Case C.G. is an example of this. (Fig. 2.)

In order to obtain excitability in the facial nerve during the course of the paralysis it was stimulated in the preauricular region, and, as a response, the contraction of the orbicularis oris was observed. The first control was carried out on the 4th day of evolution of the paralysis and the GAI was still within normal values both in the direct stimulation of the muscle and in the indirect stimulation through the nerve. The muscu-

lar response with the direct stimulation was rapid (RC). The voluntary movement (+) was weak in the frontalis and absent in the orbicularis oris (0). On the 7th day the GAI was much lower in the muscles. The orbicularis oris remained paralyzed with slow response (SC) to direct electrical stimulation but the excitability through the nerve was still present with normal GAI and a rapid muscular response (RC) to the electrical stimuli. This phase of the paralysis corresponds to so-called "partial reaction of degeneration" and its characteristics can be summarized as follows: a) accommodation index with lower values than 1.25 in the direct stimulation of the muscle and normal values in the indirect stimulation through the nerve; b) slow muscular contraction in the direct stimulation and rapid contraction as the nerve is stimulated; c) the voluntary movement is either absent or very weak.

By the 15th and again on the 29th days of evolution the signs of "complete reaction of degeneration" were observed. This is characterized by: a) low GAI values of the muscle which are close to 1.0; b) loss of the excitability of the nerve; c) slow muscular contraction to the direct stimulation; d) loss of complete voluntary movement.

By the 57th day the same characteristics described with respect to the "partial reaction of degeneration" were observed and minimal voluntary movement was in evidence. This phase has been referred to as "partial reaction of reinervation."

In about 90 days the characteristics of the normal inervated muscle reappeared. In summary these are: a) GAI values higher than 1.25 in both the direct stimulation of the muscle and through the nerve; b) rapid muscular contractions to both the direct and indirect electrical stimulation; c) normal voluntary movement.

Subgroup A-2. The patients of this subgroup had an unsatisfactory course and they did not regain voluntary movement of their paralyzed muscles (paralysis with complete reaction of degeneration not recovered). Case P.I. is representative of this group. (Fig. 3.)

By the 3rd day of evolution the values of the GAI were normal on both direct and indirect stimulation. The muscular contraction was rapid (RC) and voluntary movement was completely lost (0). On the 9th day the signs of "partial reaction of degeneration" were present. The determination of the GAI carried out on the 15th, 36th, 60th, 103rd days and later at the 10th month showed values close to 1.0.

Some speculation is justified regarding the results obtained. In both subgroups the GAI had normal values in the nerve and muscles within the first week of evolution of the paralysis. In addition the excitability of the nerve and the normal response of the mus-

FIGURE 2.

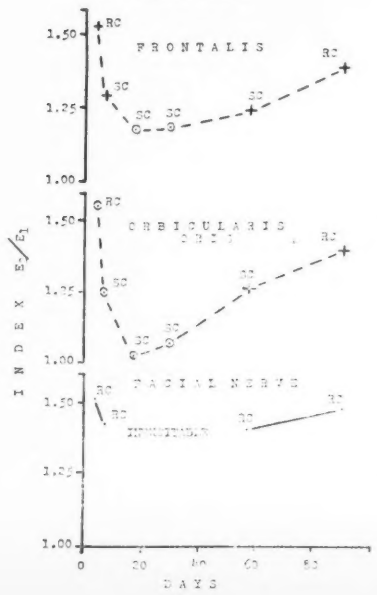

FIGURE 3.

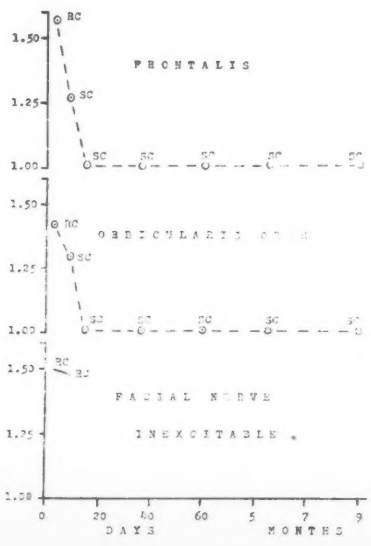

Figure 2. C.G. 45 years old. Right peripheral facial nerve paralysis (Bell's palsy). Paralysis with complete reaction of degeneration recovered. *Key to abbreviations:* + presence of voluntary movement; 0 absence of voluntary movement; RC rapid muscular response to the electrical stimuli; SC slow muscular response to the electrical stimuli.

Figure 3. Case P.I. 58 years old. Left peripheral facial nerve paralysis, due to chronic otitis, had no improvement after a course of 10 months. Paralysis with complete reaction of degeneration with no recovery.

cles to the electrical stimuli were preserved. This phase of paralysis is termed "paralysis without reaction of degeneration." The nerve excitability disappeared about 9-16 days after the beginning of the paralysis. The GAI in the nerve and muscle showed normal values for the former and progressive diminution for the latter prior to this time. This could be explained on the basis of higher excitability in the denervated muscular fibers than the enervated ones to the stimulating current, the intensity of which ascends slowly. For this reason low GAI values in the muscles and normal values in the nerve appeared in this phase of the partial reaction of degeneration. This partial degeneration could explain also the fast muscular contraction obtained as the nerve was stimulated and the slow response of the muscle as it was stimulated directly. In the first instance only the muscular fibers responded primarily because of their higher excitability to the electrical stimulation than the inervated ones.

Later as the denervation became complete (complete wallerian degeneration) there was no response as the nerve was stimulated. The GAI under these circumstances was low and the muscular contraction was slow during direct stimulation. Those cases, which showed improvement, regained a normal GAI after 2-4 months of evolution of the paralysis. At that time the muscular response was slow during the direct stimulation of the muscles and fast as the stimulus was applied to the nerve. Therefore, this kind of response under such conditions is very similar to that observed in partial degeneration and is designated as the phase of partial reinervation. In this situation the muscular fibers which have not regained as yet their reinervation showed low GAI values and slow muscular response to direct stimulation. Only the muscular fibers which obtained their re-

FIGURE 4.

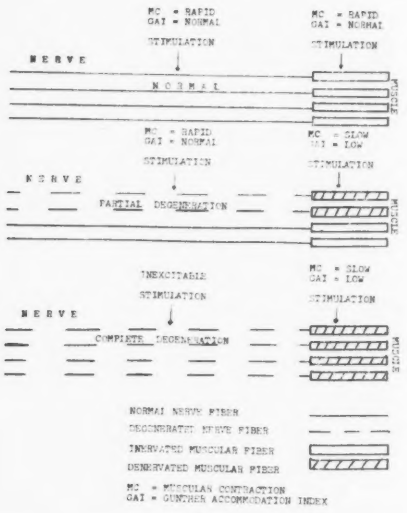

Figure 4. Schematic representation of the response of the muscle and GAI in the direct and indirect stimulation of the normal nerve and in the nerve with partial and complete degeneration.

FIGURE 5

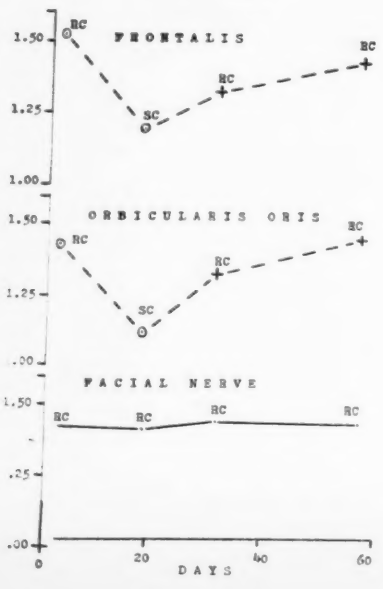

FIGURE 6

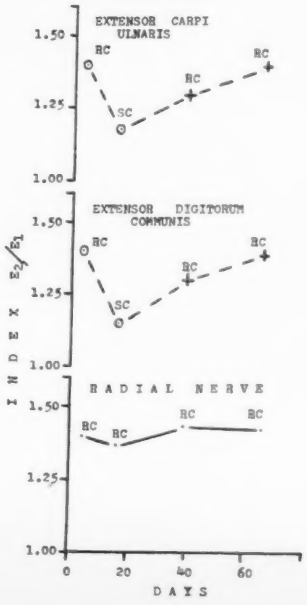

Figure 5. O.U. 13 years old. Right peripheral facial nerve paralysis (Bell's palsy) with partial reaction of degeneration.

Figure 6. D.J. 36 years old. Paralysis of the left radial nerve. Paralysis with partial reaction of degeneration.

inervation responded to indirect stimulation of the nerve with rapid contraction and normal GAI values. Later these patients regained their voluntary movements, despite the fact that some of them continued showing low GAI and slow muscular contraction during direct stimulation. This prevailed for about 2-3 weeks in some of the muscles which were paralyzed. Taboada,[7] in 1956, obtained identical results in a similar group of patients.

In the patients included in subgroup A-2 (not recovered) the evolution of the GAI was similar to that in subgroup A-1. The only exception was that the values always remained below normal once the degeneration became complete and permanent without further signs of improvement. There was obvious correlation between this observation and the poor prognosis for the paralysis. In Figure 4 the characteristics of the muscular response to the electrical stimulation and the GAI under normal conditions and in the different phases of the paralysis above described are schematized.

Group B. The patients of this group showed diminution of the GAI of the muscles without loss of nerve excitability. The cases represented by Fig. 5 and 6 show the characteristics of this group.

In patient O.U., 13 years old, with right peripheral facial paralysis, the GAI was slightly diminished in the muscles on the 19th day but by the 32nd day regained its normal value. Its values and the muscular response to the electrical stimuli through the nerve were normal throughout the course of the paralysis. (Fig. 5).

In a second patient of this group, case D.J., 36 years old, with paralysis of the left radial nerve, the GAI was slightly diminished and the muscular response was slow during direct stimulation on the 20th day, but by the 38th day regained its normal value. At that time a weak voluntary movement was noticed. By the 65th day the improvement was complete. (Fig. 6.)

The essential characteristics of the paralysis in these patients were: a) preservation of the nerve excitability during the course of the paralysis with normal GAI values on stimulation of the nerve; b) diminution of the GAI value on direct stimulation of the muscles with subsequent return to normal; c) slow muscular contraction to direct stimulation and rapid muscular response to indirect stimulation; d) recovery of function within the first two months of evolution of the paralysis.

Group C. In these patients the GAI showed normal values both in the muscles and in the nerve. The muscular contraction was rapid during the electrical stimulation throughout the course of the paralysis.

In case M. del R., 18 years old, with right peripheral facial nerve paralysis, the GAI

FIGURE 7

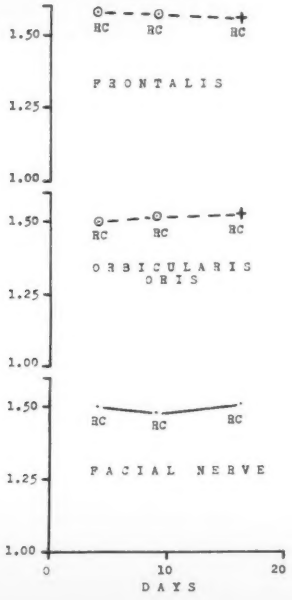

FIGURE 8

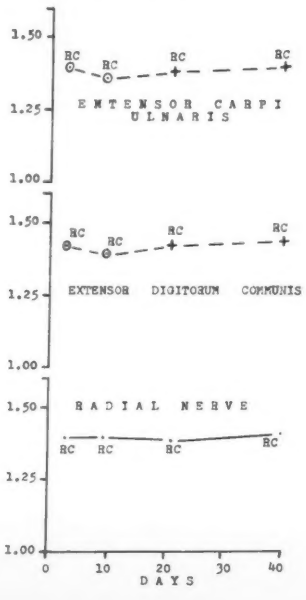

Figure 7. M. del R. 18 years old. Right peripheral facial nerve paralysis. Paralysis without reaction of degeneration.

Figure 8. R.S. 27 years old. Right radial nerve paralysis. Paralysis without reaction of degeneration.

retained its normal value in the stimulation of both muscle and nerve and there was rapid muscular contraction in response to the electrical stimulation during the entire course of the paralysis. The prognosis was good and the patient regained voluntary movement within the first 20 days. (Fig. 7.)

The other case in this group, R.S., 27 years old, with right radial nerve paralysis, showed normal values and preservation of the excitability of the nerve during the entire course of the paralysis. (Fig. 8.)

The characteristics of this group were as follows: a) preservation of the normal values of the GAI in the nerve and muscular stimulation during the entire course of the paralysis; b) preservation of the nerve excitability; c) fast muscular contraction to the electrical stimulation both direct and indirect; d) good prognosis with complete recovery within 20 days. These characteristics were similar to those observed during the first week of evolution of the paralysis in the cases of group A, before signs of degeneration were evident electrically.

Such results in these cases could be explained only by postulating a phenomenon of inhibition which impedes or blocks the passage of the voluntary impulse through the nerve. Brock[8] terms this phenomenon "neuropaxia." It could be due to a suspension of function in the fibers of the peripheral nerves resulting from such factors as compression, cocaine, and cold.

According to the results obtained in this series of cases the evolution of the GAI is correlated with the characteristic muscular response as the electrical stimulation is ap-

TABLE II—*Comparison of the Characteristics of the Three Groups Described Above. Paralyses of the Peripheral Nerves Have Been Classified Into Three Types with Respect to the Characteristics of the Paralysis Itself and the Evolution of the GAI: 1) Paralysis Without Reaction of Degeneration, 2) Paralysis with Partial Reaction of Degeneration, and 3) Paralysis with Complete Reaction of Degeneration.*

Groups	*Paralysis Without Reaction of Degeneration*	*Paralysis with Partial Reaction of Degeneration*	*Paralysis with Complete Reaction of Degeneration*
Muscular Accommodation Index (Direct Stimulation)	Normal (>1.25)	Diminished (<1.25)	Low (1.0)
Muscular Accommodation Index (Indirect Stimulation)	Normal	Normal	—
Muscular Contraction (Direct Stimulation)	Rapid	Slow	Slow
Muscular Contraction (Indirect Stimulation)	Rapid	Rapid	0
Nerve Excitability During the Course of the Paralysis	Preserved	Preserved	Disappears (Temporal or permanent)
Prognosis	Recovery 100%	Recovery 100%	Recovery (?) 57.3%

TABLE III—*Distribution of the Cases Studied and Percentage of Recovery According to the Classification Shown in Table II.*

Nerves	*Paralysis Without Reaction of Degeneration*		*Paralysis with Partial Reaction of Degeneration*		*Paralysis with Complete Reaction of Degeneration*	
	Recovered	Not Recovered	Recovered	Not Recovered	Recovered	Not Recovered
Facial	40	—	46	—	20	15
Radial	14	—	20	—	8	2
Peroneal	2	—	4	—	1	3
Sciatic	—	—	—	—	—	2
Ulnar	—	—	3	—	2	2
Median	—	—	1	—	2	—
Brachial Plexus	—	—	—	—	2	2
Total	56		74		35	26
Recovery	100%		100%		57.3%	

plied directly on the muscle or indirectly through the nerve. In the normal neuromuscular state the muscular response is rapid and the GAI has normal values (over 1.25) in both direct and indirect stimulation. These characteristics have also been observed during the first four days of paralysis, before the signs of partial reaction of degeneration are apparent, and in the course of the paralysis and the rapid muscular response to both direct and indirect stimulation were signs of a good prognosis. These patients recovered within 20 days. In cases with partial reaction of degeneration the muscular response was slow and the GAI values were low (below 1.25) in the direct stimulation, but as the nerve was stimulated the muscular response was rapid and the GAI values were normal. These electrical signs indicated a good prognosis. These patients recovered within 40 days. In cases with complete reaction of degeneration the muscular response was slow and the GAI was low in the direct stimulation. In this state the nerve became inexcitable. Of these patients only about 50% showed a good prognosis with recovery after 60 days. In this group several cases which did not recover had nerve injury and no surgical treatment. In any event, the electrical abnormalities were persistent as long as the condition remained stationary. The persistence of these abnormal electrical reactions longer than 20 days must be considered as an indication for surgical treatment of the peripheral nerve lesion.

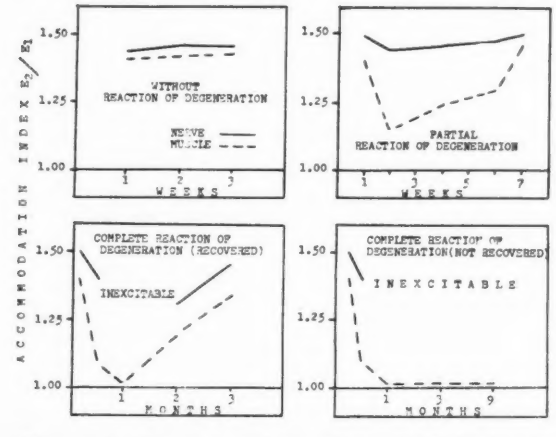

Figure 9. Average values of the GAI during the course of the paralysis determined in the muscle and nerve in the three types of evolution described in the text.

The findings above described suggest some particular points in clinical management in the following situations:

1. In cases of perpheral facial nerve paralysis (Bell's palsy) in this series, 20% of them showed complete reaction of degeneration and half of these (10%) regained voluntary movement after a period of 2-4 months. The other half showed no improvement after 10 months. Must surgical exploration be advised in this latter 10% of the cases? When should it be performed? These two questions are very difficult to answer. Two possibilities must be considered:

a) Early surgical exploration of the nerve once the signs of complete reaction of degeneration have appeared. However, in view of the favorable evolution of 10% of these cases and the operative risk involved this would appear contraindicated.

b) Late nerve exploration as the signs of reaction of degeneration persist over a period of 2-3 months. The marked muscular atrophy that would occur during this period which would interfere with complete recovery suggests, however, that this approach to the problem is also unsatisfactory.

2. In peripheral facial nerve paralysis secondary to fracture of the petrous bone, surgical exploration of the nerve is indicated as soon as the signs of complete degeneration appear. In this situation the abnormal electrical response must be considered as a result of severe nerve injury.

3. In peripheral facial nerve paralysis secondary to otitis media surgical exploration of the nerve is indicated when the signs of complete reaction of degeneration appear or persist despite the apparent cure of the infection.

4. In fracture of the long bones of the extremities with involvement of the nerves electrical exploration sometimes becomes difficult during the first few days because of hematoma formation and edema of the subcutaneous tissue. In those cases in which complications are not present or are minimal, it is possible to obtain a satisfactory result whether or not the nerve has been seriously injured. For example, in a case with fracture of the lower third of the humerus with associated radial paralysis of

less than four days' duration, the nerve should be stimulated proximal to the point where a lesion is suspected. If there is no muscular response to indirect stimulation, this suggests that the nerve has been interrupted by section or compression in such a manner that it has lost its physiological continuity. Surgical exploration is indicated despite the normal muscular response to direct stimulation and normal GAI value. If the muscle responds to indirect stimulation and the GAI is normal on both direct and indirect determination, this means that the nerve has not been seriously damaged. It is advisable then to wait and follow the evolution of the GAI and the type of muscular response. If later on, about the 16th or 20th days, the signs of complete reaction of degeneration appear, exploration is indicated.

5. In a case of paralysis associated with fracture having a duration of more than three months, if the electrical exploration at this time, without prior electrodiagnostic study, shows signs of regeneration or reinervation, physiotherapy is indicated. If the electrical study shows signs of degeneration surgical exploration must be considered.

6. If nerve paralysis appears after the fracture has been treated this suggests that the nerve has been involved by callous formation or compressed by the plaster cast. In this situation one should follow the GAI and utilize the same methods suggested in the preceding paragraph.

Summary

The exploration of neuromuscular function is described using two different types of exponential current with which two distinct thresholds are determined. The relation between them (E_2/E_1) is considered as an Index of Accommodation of the muscle and nerve (Gunther Accommodation Index).

The modification of the GAI in the course of the paralysis permits one to follow its evolution and predict its prognosis.

Acknowledgment: The author wishes to express his appreciation to Dr. William S. Fields for his assistance in the translation of this report.

REFERENCES

1. Gunther, B.: Nuevo metodo de electrodiagnostico| *Rev. Chilena de Neuropsiquiatria.* Santiago, ... *Tomo* III; 1:99, 1950.
2. Gunther, B.: Estimulacion con corriente de ascenso exponencial. *Bol. Soc. Biol. Concepcion,* Tomo VV: 115, 1941.
3. Gunther, B., y Weibel, J.: Estudio estadistico de los umbrales de la excitabilidad neuromuscular en individuos normales. *Rev. Chilena de Neuropsiquiatria,* Santiago, Tomo III: 1; 100, 1950.
4. Weibel, J.: Modificacion de la acomodacion neuromuscular en la degeneracion walleriana en el hombre. *Rev. Chilena de Neuropsiquiatria,* Santiago, Tomo III: 1; 103, 1950.
5. Weibel, J.: Influencia de la isquemia sobre el umbral y acomodacion neuromuscular en el hombre. *Rev. Chilena de Neuropsiquiatria,* Santiago, Tomo III: 1; 101, 1950.
6. Weibel, J.: Nuevo metodo de electrodiagnostico en neurologia clinica. *Rev. de Neuro-Psiquitria,* Lima-Peru, Tomo XIX: 3:362-394, 1956.
7. Taboada, J.: Indice de acomodacion neuromuscular, clinica y aspectos terapeuticos de la paralisis facial periferica. Tesis. Escuela de Medicina de la Universidad de Concepcion, Chile, 1956.
8. Brock, J.: Las bases de la clinica Neurologica. Editorial Rosario, Argentina, 1948.

Background Material of Schizophrenic Veterans

T. E. DANCEY, M.D., and G. J. SARWER-FONER, M.D.

Introduction

The purpose of this presentation is to outline a research project which it was felt would be of considerable interest, and possible import in the field of schizophrenia. The data being presented here is by no means conclusive, being a preliminary report, and represents rather the first gleanings of what it is hoped will be a large, long-term, and intensive study of many aspects of the group of schizophrenias.

In exploring for pension purposes the many applications involving schizophrenia referred to the Canadian Pensions Commission, one of us (T.E.D.) was struck by the

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repetitive pattern of neurotic and allegedly normal patients with protean variations in their symptomatology, who eventually went on to develop an illness, finally diagnosed as classic schizophrenia. The Department of Veterans Affairs district files and Army documents contain much data on the overall functioning of patients during service, as well as the complete medical documents on hospitalizations, and O.P.D. follow-up, etc.

A study of a specially selected group of patients with classic and unquestionable schizophrenia by Bleulerian standards, in that all the secondary signs and symptoms of the illness were present was therefore suggested. All had developed schizophrenia either directly while in service, and were therefore discharged and pensioned, or had been discharged with a non-schizophrenic diagnosis, i.e., either as apparently normal, or with a neurotic diagnosis, but had in the post-discharge years developed schizophrenia. These latter cases, of whom 2,400 are known to date, were pension applicants to the Canadian Pension Commission. Unreconstructed data and case histories exist on all of these in our Army and D.V.A. documents. This is in contradistinction to the usual anamnesis of the schizophrenic patient in being *pre hoc* rather than *post hoc*. This data could, it was felt, offer important clues on the pre-schizophrenic functioning and personality, as well as partial evidence based on original, unreconstructed, and spontaneous observations on the type of circumstances and events that led to the schizophrenic break-down.

Perusal of the files made it amply clear that adequate data on the family, and developmental history was not available. It therefore became necessary to study the family life of the schizophrenic veterans. There are two phases to this and only the first phase is included in this report. It consists of a good psychiatric anamnesis with special accent on the family interpersonal relations, and familial atmosphere.

It was hoped to be able to separate all seemingly pertinent points into factors, and classify these when a large enough series to make this feasible was obtained. A check sheet for, and way of organizing, such data is a byproduct of this study, and will be presented elsewhere.[2] Data as to cultural and social factors, intracultural conflicts and stresses, as well as on genetic and morphological, i.e., body type, aspects of these patients and their families will be collected as it becomes available. A limited quantity of this type of data is available for presentation here.

Hypotheses: Based on clinical experience, the authors had prior to this study believed that in male schizophrenic patients:

1) Profound difficulties in interpersonal relations in the family group would be found in all schizophrenic patients.

2) These difficulties, it was felt, would indicate profound degrees of disturbance in the schizophrenic patient from birth onward, with either overtly cold, hostile, and rejecting mothers, or subtly overprotective but hostile, rejecting mothers; as well as weak, passive, or absent fathers.

3) The authors felt that the schizophrenic patient was not encouraged to reach out to his environment for gratification of his needs, since his life experiences from the earliest age with the significant humans of his group had taught him that he would be largely frustrated. A withdrawal of energy from these painful contacts, and an incomplete introjection and mastery of his environment and himself results.[3]

4) Both authors felt that much evidence in favor of the psychoanalytic hypothesis of the continuum of ego defences might be forthcoming, since in the evolution of the illness one could in many cases clinically see the gradual break-down of "normal" and "neurotic" defences of a higher order into grosser, more imperfect, "lower order" of defences,[4] and finally into a fragmentation of the ego, i.e., a break-down in reality contact and reality testing.

5) Based on war experience and the work of such authors as D. G. Wright,[5] and D. O. Bond,[1] it was felt that there should be much evidence for the personal specificity of traumatic occurrences in the adult life of such a patient. These events would have to have a personalized traumatic significance for that individual. Such events would have to strike at vulnerable areas in the personal-

ity, which were affectively linked with the concept of self, of manhood, or of body image. These symbolically linked occurrences would, therefore, be linked with affect-laden areas of conflict in psychosexual identification and fixation in psychosexual development. For the events of daily living in adult life to be traumatizing, it was theorized that these occurrences would have to coincide in time with crucial life situations, giving them the opportunity to strike the vulnerable terrain of the particular individual. We felt that fate often takes a hand, and a heavy one at that, in many of these illnesses.

The above hypotheses were based on earlier and considerable clinical experience with schizophrenia, and it was felt that the data would offer a particularly rich source of study in terms of the ego defences, the process of breaking down into a schizophrenic episode, and of remitting from it.

Resuméd Findings: The District Files of 100 male schizophrenic veterans of the Canadian Armed Services were studied by the psychiatric portion of the team. A smaller number of these patients' family structure, and the patient's developmental history in that family have so far been studied. This work is continuing.

The evidence that is listed below consists of the trends and tendencies that have so far appeared. Further study of a larger series is necessary before definitive conclusions can be drawn.

Trends Shown by the Study to Date: (It is to be remembered that all of the subjects of this study are males).

1) Adult or adolescent life experiences generating ego shattering anxiety[5] were always linked with experiences which had the ability to reawaken deeply-rooted feelings of personal inadequacy, worthlessness, and therefore produced feelings of perversity as well.

2) These "accidents of everyday life" seem to need a timing of individual significance for that patient, in order to act as a shattering experience.

3) These life experiences achieve a traumatic and shattering significance only when their meaning to the patient is one shattering the patient's own concepts of self, body image, and psychosexual identifications.

4) There was always uncertainty and conflict in the patient's mind about his concept of self, of his body image, and of his psychosexual identifications. These uncertainties were based on developmental experience in his own family.

5) When his adult compromises with these conflicts no longer sufficed, feelings of uncertainty, ambivalence, weakness and, as a result, perverseness were generated.

6) It is these latter that seem to generate the intolerable anxiety[6] leading to a giving up of the externalized contacts that provoke these feelings.

7) The traumatic experience in his life always seemed to refer back to evidence visible in our family study, and in the psychodynamics of the individual patient to several constant factors:

(a) An inversion of roles between mother and father, in which mother was the stronger, more domineering, and capable person; while father was often a kinder, weaker, more permissive, aloof, quiet, or generally absent figure.

(b) A variant of the above, but with the same significance for the patient, was a kindly, overprotective mother, with much subtle and latent hostility towards men, who has a symbiotic relationship with a weak and infantile father to whom she gave, and from whom she received, and who had little love or attention, but much ambivalence, rejection, and hostility left for the patient concerned.

8) When the last-mentioned factors were combined with either a cold, undemonstrative, mother with marked inability to give or with a mother who had greater capacity to give to others, but who specifically rejected, for varying personal affects, the individual concerned from birth onward—an offspring developed with marked conflicts, and ambivalence over his own adequacy, acceptability, suitability, or normalcy. From his earliest days such a person was not encouraged to reach outward for gratification of his instinctual needs, since they were all too often frustrated. The crucial differentiating feature hypothesized by the authors here is the fragmentary and incomplete mastery of the world (poor introjection), and of his body; the looseness of the affective relations,

and the lability and ambivalence of the latter. This occurs since this constellation leaves no solid basis for contacts with reality, or for a feeling of personal ability to enable him to stand up to the struggles of later life.

9) In terms of our interest in ego defences, the constant presence of neurotic defences, and the use of successive series of them to attempt to cope with, and compromise with the conflicts, is a noteworthy feature. The gradual changes in behavior under the stress of circumstances which challenge the defences, by creating conflicts of great intensity over ego ideals, over visualization of self, over sexuality, over social adequacy, or over any one of a dozen areas of the social representation of a man's roles in life, is easily followed.

10) A poorer level of defences then supercede the original ones, and the period preceding the overt occurrence of the schizophrenic's illness is characterized by normal, neurotic, border-line (acting out), psychosomatic, as well as medical and surgical manifestations of disturbance.

11) Common adult experiences of specific ego shattering significance to the individual patients were seen, such as V.D., injury, or a wound. Adult life experiences such as threat of engagement, marriage, pregnancy, or the birth of a child; distress at being in an all-male group (with resulting stimulation of latent homosexuality); years of marital life with a domineering female, when the male concerned had marked doubts about his own masculinity to begin with, with the resulting development of a gradual feeling of castration or loss of masculinity occurs with a slow spread to social areas such as work, etc.

It is to be emphasized that much more work will have to be done before the above-mentioned trends and tendencies can be affirmed to be vital. They are mentioned here because they are the trends which have appeared to date.

Conclusions

Thus, many interesting areas of pre-schizophrenic functioning, of data on the family interpersonal relations, as well as on the break-down in ego defences, and their restoration are offered in this study. It is visualized that the patient begins with a biological, genetic endowment at birth, and that life experiences beginning at birth, and based on the family interpersonal relations mold, modify, and seem to be of marked import in the development, or in avoiding development, of a schizophrenic illness. We have elaborated an holistic theory of schizophrenia.

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REFERENCES

1. Bond, D. D.: The Love and Fear of Flying. *Intern'al Un. Press,* 1952.
2. Sarwer-Foner, G. J., Dancey, T. E.: A Technique for Charting Factors of Possible Significance in Schizophrenia. *In Preparation.*
3. Sarwer-Foner, G. J.: Some Theoretical Considerations on the Modes of Action of the Tranquilizing Drugs in Schizophrenia, in "Psychopharmacology Frontiers," Proc. Psychopharmac. Symp., 2nd Int. Cong. Psychiat. 1957. Edit. N. S. Kline, p. 295-303, and Disc. p. 445-446, 476. *Little, Brown,* Boston, 1959.
4. Sarwer-Foner, G. J.: Psychoanalytic Theories of Activity-Passivity Conflicts, and of the Continuum of Ego Defences: Experimental Verification Using Reserpine and Chlorpromazine. *Arch. Neurol. Psychiat.,* 78:4, 413 (Oct.) 1957.
5. Wright, D. G.: In First Year Experience in Combat with the 8th U.S. Air Force. *Josiah Macy Jr. Foundation,* New York, 1943.
6. Wright, D. G.: In Psychotherapy with Schizophrenia—A Symposium. Edited by Brody and Redlich. *Intern'l Un. Press,* 1952.

The Isolated Cerebral Seizure

(Report of Five Cases)

ROGER MERRITT MORRELL, M.D.

Introduction

The isolated cerebral seizure without sequel or previous convulsive history is a distinct medical problem. A convulsion is a response to injury and is not diagnostic as to cause. The number of diseases, whether genetic, vascular, inflammatory, traumatic, metabolic, or neoplastic, affecting cerebral structures are numerous; the incidence of epilepsy is two out of 100.[1] The convulsion is produced by ganglion cell discharge in gray matter.[2] The location of the discharge determines the aura or seizure pattern, which may be in visual, auditory, olfactory areas, psychical or postural as well as the motor seizure commonly associated with the term "epilepsy."[3,4]

Physiological responses to stimulation do not correspond necessarily to cyto-architectonic areas (e.g. Brodmann). Post-rolandic sulcus discharges may give purely sensory changes progressing up or down the body, but constitute a seizure just as much as those which produce motor progression from the pre-rolandic sulcus.

Sensory manifestations may occur on the side of the cerebral lesion or bilaterally, due to activity of primary or secondary sensory area.[5] In a patient whose seizures were on the left side of the body, ipsilateral or bilateral sensory responses were obtained. A glioma was found along the superior bank (frontoparietal operculum).[6]

Just anterior to the paracentral gyrus is the "supplementary motor area." Stimulation or seizures here produce head adversion. The opposite upper extremity is held above the head and the eyes seem to look at it. The contralateral foot is extended. Stimulation or a seizure here on the dominant side will arrest speech. Speech disorders may be the first manifestation of a seizure and are of as much localizing significance as movement. In seizures emanating from the calcarine fissure, circular colored lights may appear in the field of vision contralateral to the attack or stimulation. Anterior to this along the temporal lobe, such visual phenomena may arise in both fields, but here they are usually rectangular and black and white. Here also, one may elicit adversive eye movements.

Temporal lobe disorders may be divided into those of audition and vertigo, smell and taste, and psyche and perception. These all have localizing value and may be induced by epileptic discharge or stimulation. Of particular importance are psychomotor abnormalities, perseveration and loss of recent memory. The seizure may release psychopathic behavior (patients "controlled" with phenurone may have more behavioral abnormalities than before therapy). This may also be noted after temporal lobotomies,[7] and is a question of importance in judging potential psychological calamities resulting from therapy.

Cerebral seizures need not produce movement. The work of Magoun, Penfield, Cairns, etc., has shown that centers related to level of consciousness lie in the reticular substance and intralaminar nuclei of the thalamus along the entire brain stem. Primary ganglionic discharge in such structures may produce only a transitory loss or interruption of consciousness. Such patients cannot be labeled petit mal without three per second spike and wave on EEG and the "petit mal triad," i.e., absence akinesis, or myoclonic pattern. Also, a tumor superficially located may spread centrally and produce a transitory lapse of consciousness (clinical "petit mal") or it may spread over the convexities producing generalized clonic movements ("grand mal"). Similarly, the dysrhythmia of patients with the three per second spike and wave may spread to the surface and give generalized seizures. Thus, grand mal and petit mal are purely descriptive terms, do not add to knowledge of the disease, and are used differently by different workers. The

From U.S. Public Health Service Hospital, Staten Island, New York.

term "cerebral seizures" appears to be more accurate and less confusing.

Case Reports

The following reports describe single seizure patients at the Johns Hopkins Hospital.

Case 1: 31 year old white male.

Past History. Sterilization age 16; mastoidectomy age 8; German measles. Fairly well developed but mentally retarded (I.Q. 90—did not talk or walk until age 2). Mother's labor was 40 hours in length; high forceps delivery with cranial injuries. Head enlarged as a child. Questionable hydrocephalus or macrocephaly.

Present Illness. Three weeks prior to admission during a bridge game, the patient leaned forward, felt constriction in the throat, inability to swallow, heaviness of the tongue, wanted to speak but was unable and eventually slumped to the floor without convulsive movements. He recovered consciousness without urinary or fecal incontinence and had no post-ictal symptoms of note. There was no aura.

Physical Examination. Obese, white male of strange, dwarf-like appearance. Head was large, square, without exostoses, but there were unusual longitudinal ridges 1 to 2 cm. apart on the superior aspect of the cranium. Scalp moved freely over these ridges. Eyes were prominent. Teeth somewhat separated above everted lips. The tongue was large. The neck was beset by fat pads. Thorax barrel-shaped. Neurological examination normal.

Laboratory Data. EKG showed left axis deviation. Neurological impression was that this was primary macrocephaly with questionable compensated hydrocephalus. Air studies contraindicated because of the possibility of stimulating the choroid plexus to overactive production of cerebrospinal fluid. Patient was discharged on 32 mgm. sodium phenobarbital q.i.d. and Dilantin 90 mgm. once a day.

Case 2: 52 year old white male.

Present Illness. The patient arrived home from work one evening feeling more tired than usual. He noted weakness and fatigue on climbing the stairs, and had to lie down. He got up, later started to disrobe, but felt weak and sat on a chair. According to his wife, he then slumped to the right. In a few seconds, he stiffened in a tonic seizure followed in turn by clonic movements of the upper extremities and deep respirations. There were no chewing movements or incontinence, and his eyes were rolled upward. He remained unconscious on the chair for five minutes. On recovering he felt relaxed, fatigued, and did not realize he had lost consciousness. He slept through the night. One month preceding the episode, he had noted injection of his right eye, with sandpapery sensations, and increased sensitiveness of the forehead above this eye. For 30 years, he had noted occasional "twirling" sensation in this eye. No ocular difficulties followed the first seizure. Afterward he felt fatigued for two to three days and slept more than usual during the day. His wife thought his voice more nasal in quality during recent weeks. Three days later, the patient and his wife were reading, and she noted he had a dull expression and partly opened mouth. EEG and visual fields at Bethesda Naval Hospital were within normal limits. Re-examination of the eyes following the seizure revealed the right pupil smaller than the left.

Physical Examination. Right palpebral fissure appeared narrower than the left. Heart sounds: P2 slightly louder than A2. Neurological examination revealed a slight droop of the right lid (present for years); hypoactive gag reflex; reflexes slightly hypoactive, symmetrical throughout.

Ophthalmological Examination. Myopia with astigmatism, presbyopia.

Neurological. Consultation: "Common problem of a single fit in an adult without other evidence of neurological disease. Differential includes: (1) focal discharging lesion, (A) tumor or other expanding lesion; (B) scar (etiology unknown); (C) focus of late onset. (2) metastatic disturbance: (A) hypoglycemia; (B) alcohol or drug. (3) cerebrovascular disease. (4) cerebral atrophy (Alzheimer's disease). If he has a tumor it is in essence operable or inoperable now and will be no more or less so months from now, when signs may be much clearer."

Laboratory Data: Total eosinphil count, 176 per cubic mm. (8% eosinophilia on differential count of white blood cells). Otherwise negative. *EEG.* Short bursts of sharp waves and slowing, especially in left temporal tip. Definite seizure pattern noted on hyper-ventilation. It was felt this might represent a deep-seated non-cortical lesion. He was started on anti-convulsive medication consisting of Dilantin 100 mg. three times a day, phenobarbital 100 mg. at bedtime. No major or minor convulsive episodes occurred during hospitalization.

Disposition. To continue anti-convulsive therapy with re-evaluation at three to six month intervals.

Case 3: 44 year old white male.

Chief Complaint. Unsteady gait of 9 months' duration and diplopia of 6 weeks duration.

Family History. Positive for diabetes mellitus, heart disease, cerebral vascular accident, and alcoholic cirrhosis.

Past History. Sudden onset of right facial paralysis, clearing in a few weeks without residual. In February 1954, he noted onset of unsteady gait progressive until present time. Unsteady gait with increase of unsteadiness when dark or attempting to change direction. Legs were "stiff." The patient noted impairment of memory and concentration. On 5-26-54 he had a convulsive seizure without aura, awakening the next morning in hospital. Lumbar puncture and EEG were normal and he was discharged. Six weeks prior to admission he noted onset of double vision, disappearing when using eyes separately.

Physical Examination. Moods vary between depression and gay tension. Pupils react sluggishly to light and accommodation; slight nystagmus of

small amplitude upon extreme lateral deviation; diplopia during left conjugate gaze; left palatine arch lower than right.

Neurological Examination. Speech was somewhat slurred. Gait was unsteady; walked with broad base. Heel to knee test bilaterally impaired. Finger to nose performed well. No past-pointing. Romberg positive to right. No motor weakness, wasting, atrophy or fasciculation. Muscles of lower extremities have adequate tone. Achilles and quadriceps reflexes bilaterally brisk and hyperactive. Nystagmus: horizontal with a rotary component. No ankle clonus, but positive Babinskis bilaterally. Numbness in the legs but normal responses to pin and tuning fork and position sense tests. Initial impression: multiple sclerosis.

Ophthalmological consultation revealed low grade paresis, right inferior rectus and questionable paresis, right superior rectus, with no acuity change.

Electroencephalogram normal.

Lumbar Puncture. Negative CSF Wasserman. 58 red cells and one white cell in spinal fluid. NPN 30. WBC 10650. Differential: 1 juvenile neutrophile, 72 segmented neutrophiles, 2 eosinophiles, 1 basophile, 21 lymphocytes, 3 monocytes. After 10 days of isoniazid therapy (75 mgm. t.i.d.) the patient denied double vision, and there was no nystagmus. Station was nearly normal, but gait was still ataxic. Left heel to knee test well performed. Babinskis still present. There was a marked change in mental state from profound depression to near euphoria. EKG: Left axis deviation. Discharged improved on 50 mgm. t.i.d. of isoniazid.

Case 4: 16 year old female.

Family History. Negative.

Past History. Health good except for respiratory allergy.

Review of Systems. Mild headache lasting one hour, after fainting.

Present Illness. In spring 1948 she had a "fainting spell" attributed to overdose of ephedrine and benadryl taken for asthma. She has had three subsequent "spells," (Nov. 1948, Feb. 1949, June 1949). The attacks are similar: She is "fatigued," blacks out, recovers promptly within a minute and feels well except for "tightness" in the head, lasting an hour. She fell once, bumping her head. These attacks have occurred roughly three hours after eating. When she arises suddenly she frequently feels giddy.

Physical Examination. Blood pressure, reclining 96/50, sitting 84/44. One small posterior cervical node.

Neurological. 24-hour starvation produced hunger but no fainting. Twenty minutes after 100 gm glucose orally she felt nervous, and perspired. The same reaction followed seven minutes after injection of 0.3 mg. of adrenalin. EEG: Basic pattern 9 per second waves in all leads, with some 7 to 8 per second frequencies, and no seizure discharges or focal signs. Marked buildup on hyperventilation, with 3 per second high voltage waves (short spikes). Impression was normal EEG in resting state, atypical petit mal discharge produced on hyperventilation. She was placed on Dilantin, 90 mgm. three times a day, to be augmented with Tridione as necessary.

Follow-up. On February 14, 1952, white count 9700, differential showed 5 atypical lymphocytes, 78 lymphocytes, 11 neutrophiles, 4 juveniles. Heterophil agglutinations positive 1/640. *Liver Function Tests:* Cephalin flocculation two plus, thymol 6.2, others normal. Anti-epileptic medication had been continued up to and including this period with no events.

Follow-up. December 28, 1954. At age 22, EEG showed low-voltage slowing at rest, definite sensitivity to hyperventilation, but no prolonged return. Nothing of spike and wave pattern. It was, however, outside limits of normal for the age. In view of absence of clinical convulsive episodes, at this time, medication was tapered. Record repeated one month after cessation of medication.

Case 5. 44 year old white male bar manager.

Chief Complaint. Single convulsive seizure.

Family History. Diabetes in mother, who also had a non-toxic goiter biopsied but not removed. Paternal grandfather had cancer of throat.

Past History. Negative.

Review of Systems. Paroxysmal nocturnal dyspnea accompanied by anterior chest pain.

Present Illness. In past 10 years, had 4 to 5 attacks of sudden inability to move the left hand. This lasted minutes without sequelae. For 1½ years prior to admission had episodes of numbness of right hand and arm and right leg and foot. The night prior to admission he collapsed without warning and struck his head over the left eye. He was found by his wife with limbs rigid and head and shoulders moving rhythmically, the left hand drawn up in flexion. He came to in 10 minutes, was aphasic for a few minutes, and had amnesia for the whole event. No history of syncope.

Physical Examination. ..Left costal margin higher and more protruding than right. Some diffuse abdominal guarding. Impression: neoplasm, involving left cerebral cortex, or static condition such as a scar, cyst or malformation of vascular structures. There was left cardiac ventricular enlargement.

Laboratory Data: Air injection, left carotid arteriogram, and lumbar puncture negative. NPN 31. FBS 80. WBC 5,950. Differential: Segmented neutrophiles 60, eosinophiles 30 basophiles 2, lymphocytes 31, monocytes 4. EKG: Left axis deviation, slight.

Electroencephalogram. Patient received 1.5 gm. chloral hydrate before EEG. "Late record shows predominant frequency of 10 per second, clearest in occipital poles. There is a very moderate low voltage fast activity in the background in all areas. There is a mild but consistent voltage asymmetry with lower voltage in the left low central area and in the right, interpreted as being normal. No seizure discharges on hyperventilation and alterations." Patient was to return for periodic examinations.

Discussion

It is apparent that initial clinical phenomena are of extreme localizing importance. The patient and relatives should be questioned in detail concerning these. They should be looked for as soon as the aura occurs since the seizure may cause an amnesia for the aura, movement or sensation. The progress of the seizure should be minutely noted. Afterward an immediate neurological examination, including visual fields, cortical sensation and speech may reveal a post-ictal paresis (Todd's) which may be of localizing value.

Etiology. A progressive lesion after age 21, even without headache and papilledema is tumor until proven otherwise. Pituitary tumors strike the uncus early and 25 per cent have uncinate fits. Infection must be ruled out (e.g. lues), metabolic disturbances checked, and histories of birth trauma and other injuries[8] must be investigated thoroughly. Cardiac arrhythmias, old vascular lesions and subacute bacterial endocarditis must be ruled out. Only after an adequate anatomical localization and every attempt to determine the pathogenesis have been made, may one consider therapy.

Therapy. Therapy of seizures must be directed to the cause. In tumor or abscess, surgery is usually indicated. When secondary to vascular disease, the primary pathology must be treated. In most seizures non-expanding lesions, scar formation, and hereditary factors play dominant roles. In these cases, therapy must be directed to the seizure pattern and not to removal unless medical therapy fails. Treatment is dependent in all cases on reducing the frequency of abnormal ganglionic discharges. Bromides and barbiturates are effective and soporific.

Putnam and Merritt (cited in 9) introduced the hydantoin derivatives (Dilantin and Mesantoin); 4½ grains daily with minimum doses of barbiturates give control in most convulsive problems. Tridione may be useful in three-per-second spike and wave patterns which do not respond to Dilantin and phenobarbital. Drawbacks to the use of the hydantoin group are skin reactions and cerebellar disturbances. Any skin manifestation following hydantoin administration is an indication for immediate cessation of the drug, since fatal exfoliative dermatitis may ensue.

In the dione group, agranulocytosis also occurs. Phenurone has been discontinued for temporal lobe seizures because of this and psychiatric complications. The latter, however, are probably due to the effectiveness of the therapy. Candidates for surgery are patients with focal seizures, firing from a single area (EEG), focal signs, and lack of medical response.[19] Surgery in such patients (1-3% of epileptics) gives a 56 per cent chance of freedom of seizures. In all seizure patients socioeconomic considerations are of great importance.[20]

Research Progress. Spontaneous seizures are due to neuronal hyperactivity. A basic lesion and/or multiple factors may operate to produce the discharge.[10] Such a lesion might be situated in one of the two principal "compartments" of neuronal metabolism: (1) energy metabolism, concerned with the neurone's vital integrity; (2) activity metabolism, concerning its functions of conduction.

Energy metabolism is important because of the virtually exclusive dependence of nervous tissue upon carbohydrate and oxygen. In contrast to other active tissues (e.g. liver or muscle), nervous tissue cannot function effectively under anaerobic conditions and on energy derived from lipids. During a seizure, changes occur which are consistent with increased demands for energy but no significant abnormalities between or prior to seizures were observed. Elliott has concluded that, while convulsive activity imposes an excessive demand upon the energy-producing mechanisms of brain tissue, there is no indication that derangement, of, or interference with the energy-producing potentialities is necessarily concerned. Nevertheless, it is difficult to conceive of a lesion which does not involve energy systems.[11]

Acetylcholine may be responsible for many, if not all, central neuronal transmission seizures. Acetylcholine occurs in high concentration in nervous tissue together with enzyme systems for its production (choline-acetylase) and for its rapid inactivation (acetyl-cholinesterase). It exhibits convulsant properties at minute concentrations. It

has been demonstrated (a) that in focal epileptogenic lesions acetylcholinesterase activity is elevated; (b) that detectable amounts of free acetylcholine are present in the CSF of epileptics (whereas it is rarely found in non-epileptics); and (c) that anticholinesterase toxicity is often characterized by seizures.[12] There is a "significant" abnormality of acetylcholine metabolism in focal epileptogenic cortex, persisting *in vitro* under optimal incubation conditions. In epileptics excess free, active acetylcholine may be produced instead of the minute increments associated with physiological activity. Increased cholinesterase activity locally (presumably compensatory), free acetylcholine in cerebrospinal fluid, and experimentally increased free acetylcholine in fluid from the cortical surface during seizures support this suggestion. The possibility of such an excess being concerned with initiation of the seizure discharge awaits further study.

In vivo anesthetics and anticonvulsants counteract the failure of epileptogenic tissue to bind acetylcholine. The *in vitro* addition of glutamine, asparagine or A.T.P. (but *not* glutamic acid) reverse this defect, apparently due to alteration of metabolic activity. Energy from A.T.P. is necessary to maintain intracellular glutamic acid, glutamine, potassium ions, and probably bound acetylcholine, and is required for glutamine synthesis.

The glutamic acid level is significantly lowered in focal epileptogenic cortex.[13] This *metabolic* defect can be reversed *in vitro* by addition of asparagine, glutamine, or A.T.P. Recent studies indicate that such tissue may not be able to maintain a normal potassium concentration.[14]

The biochemical lesion in focal epileptogenic cerebral cortex involves most of the important neuronal metabolic systems. Glutamic acid occupies a peculiarly vital position in this scheme situated as it is at a metabolic cross-roads between intermediary carbohydrate metabolism (through equilibrium with alpha-keto-glutarate of the Krebs tricarboxylic acid cycle) and protein metabolism (via transamination reactions). In addition, glutamic acid and glutamine constitute the major anions of neurones and appear to be concerned with the movement of potassium ions, which are directly concerned with membrane polarization and impulse conduction.[15] Aspartic acid may occupy an analogous position in metabolic interconversion.

Pyridoxal phosphate, a coenzyme derived from pyridoxine (vitamin B_6) catalyzes these reactions. Its relationship, and that of acetylcholine,[16] to the other biochemical systems, is not clear. The relationship of carbonic andhydrase[17] and corticosteroids[18] to seizures is not well understood.

Summary

1. The present clinical concepts regarding cerebral seizures are briefly outlined.

2. Five cases of isolated cerebral seizures in adults are presented, illustrating schemes of diagnosis and management.

3. Trends of research in cerebral seizures are outlined.

BIBLIOGRAPHY

1. Caveness, W.: Survey of Public Attitudes Toward Epilepsy. *Epilepsia,* 4:19-26, 1949.
2. Jackson, J. H.: A Study of Convulsions. *Tr. St. Andrew's Grad. A.,* 3:1-1870.
3. Penfield, W., and Humphreys, W. S.: Epileptogenic Lesions in the Brain. *Arch. Neurol. and Psychiatr.,* 43:240, 1940.
4. Penfield, W., and Jasper, H.: Epilepsy and the Functional Anatomy of the Human Brain. Boston, Mass. *Little, Brown Co.,* 1954.
5. Woolsey, C., and Penfield, W.: Patterns of Localization in Precentral and "Supplementary" Motor and Sensory Areas and Their Relation to the Concept of the Premotor Area. *A. Res. Nerv. & Ment. Dis., Proc.,* (1950), 30:238-264, 1952.
6. Shy, G. M.: Unpublished Observation. 1954.
7. Bailey, P.: Concerning Neurology and Psychiatry. Introduction, 1948. Yearbook of Neurology, Psychiatry and Neurosurgery, Chicago, 1949, *Yearbook Publishers,* p. 493.
8. Livingston, S.: The Diagnosis and Treatment of Convulsive Disorders in Children, 320 pp. Springfield, Ill., *Thomas,* 1954.
9. Toman, J. E. P., and Taylor, J. D.: Mechanism of Action and Metabolism of Anticonvulsants. *Epilepsia,* 1:31-48, 1952.
10. Tower, D. B.: Nature and extent of Biochemical Lesion in Epileptogenic Cerebral Cortex: Approach to Its Control *in Vitro* and *in Vivo.* Presented before the annual meeting of the American Academy of Neurology, Washington, D.C., May 1, 1954.
11. Elliot, K. A. C., and Penfield, W.: Respiration and Glycolysis of Focal Epileptogenic Human Brain Tissue. *J. Neurophysiol.,* 11:485, 1948.
12. Tower, D. B., and Elliott, K. A. C.: Experimental Production and Control of Abnormality in Ace-

tylcholine Metabolism Present in Epileptogenic Cortex. *J. Appl. Physiol.,* 5:375-391, 1953.
13. Weil-Malherbe, H.: Glutamic Acid and Its Relation to Nervous System. In Metabolism and Function in Nervous Tissue: A Symposium held at the London School of Hygiene and Tropical Medicine on November 10, 1951. Edited by R. T. Williams, 102 pp. London: *Cambridge University Press,* 1952, pp. 16-26.
14. Terner, C., Eggleston, L. V., and Krebs, H. A.: Role of Glutamic Acid in Transport of Potassium in Brain and Retina. *Biochem. J.,* 47:139-149, 1950.
15. Brink, F., Jr.: Role of Potassium in Activity of Nerve Cells. *Journal-Lancet,* 73:171-173, 1953.
16. Feldberg, W.: Role of Acetylcholine in Central Nervous System. *Brit. M. Bull.,* 6:312-320, 1950.
17. Merlis, S.: Carbonic Anhydrase Inhibitor: Its Use in Epilepsy. Presented at a joint meeting of the American Academy of Neurology and the American League Against Epilepsy, Washington, D. C., May 1, 1954.
18. Lowell, J. M., et al.: Convulsive Seizures. *New Engl. J. Med.,* 244: 2-50, 1951.
19. Smith, B., and Forster, F. M.: Role of Some Experimental Anticonvulsants, Mysoline, Milontin and 1461-L.M. *Ann. Med. Soc. District of Columbia,* 22: 279-282, 1953.
20. Lennox, W. G., and Markham, C. H.: Sociopsychological Treatment of Epilepsy. *J.A.M.A.,* 152:1690-1694, 1953.

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Pharmacologically Induced Parkinson Like Signs as Index of Therapeutic Potential

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The advent of pharmacological success in the treatment of emotional disorders has brought with it increasing comment on the prevalence and clinical value of extra-pyramidal signs among treated patients. Some investigators[1,2] have stressed either the therapeutic value of the extra-pyramidal signs or the alleviation of such signs while others[3] have distinguished only trends or equivocal evidence at best. The inconsistent nature of these reports has prompted the controlled study reported here. The intent was to study the therapeutic outcome of prolonged induced extra-pyramidal signs as opposed to the possible beneficial change in behavior accompanying control or absence of these signs. The pharmacological agents under study here are Trilafon (perphenazine) and Cogentin (benztropine methanesulfonate). The former was selected not only because of its reputed high therapeutic potency,[4] but also because of its chief side-effect—Parkinson-like signs. The latter was selected because of possible speculation regarding its incidental "tranquilizing" effect and its ability to control pharmacologically induced extra-pyramidal signs.

From Evansville (Indiana) State Hospital.

Method

The group under study constituted an entire psychiatric hospital ward of chronically psychotic women whose median age was 51 years with a median hospital residency totaling 13 years. After three patients (2 chronic brain syndromes, 1 suspected mental deficient) were eliminated from consideration, the sample comprised 40 subjects who were sorted at random into five categories.

Group I—Five patients received Trilafon placebo.

Group II—Five patients received Cogentin. One of these patients expired three weeks later due to an ongoing deterioration process.

Groups III, IV, and V—Thirty patients received Trilafon, in rapidly increasing dosages from 32 mg., to 48 mg., to 64 mg., to 96 mg., to 128 mg., daily so as to reach the maximum level within a 14 day period, with the expressed intent of producing extra-pyramidal signs in as many cases as possible. However, so as to lessen the possibility of "hangover effect" a preliminary two week period was established during which all medication and somatic therapies were withheld. Increments in dosage levels were effected simultaneously for all patients. All patients were evaluated daily for Parkinson-like behavior by the senior author. A total of nine patients (30%) developed extra-pyramidal signs, one of them, aged 75, being removed from the study almost immediately due to medical considerations not associated with the induced signs. The group

showing Parkinson-like signs was divided alternately into two groups (III and IV) paired in accordance with order of onset of symptomatology. One member of each pair received sufficient Cogentin (in addition to the dosage of Trilafon necessary to produce extra-pyramidal signs) to control the symptoms. The other Parkinson-like patients were maintained on the minimally effective dosage producing these signs. The remaining 21 patients (Group V), with a single exception, were continuously maintained on the prescribed dosage level. The single exception involved a 78 year old who, after reaching 128 mg. daily, was rapidly brought down to 16 mg. daily and maintained at this level. The rapid decrements in dosage were prompted by furthered immobilization in a very sedentary woman. At no time did she show extra-pyramidal signs.

To guard against undesirable side-effects a base line was established consisting of blood pressure, complete blood count and urine examination for bilirubin.

Weekly behavior ratings were performed on each patient by the ward nurse with the assistance of the junior author. The raters were at no time aware of the medication being received by any particular patient. Each patient was rated along four separate behavior scales: 1. affect; 2. communication (both are sub-scales of the MACC Behavioral Adjustment Scale by Ellsworth); 3. perceptual distortion; 4. conceptual disorganization (both are sub-scales of the Multidimensional Rating Scale for Psychiatric Patients by Lorr). The following are illustrative samples of the kinds of items comprising these scales:

(1) Is he pleasant, never seems to be irritable or grouchy?

(a) Usually very grouchy.
(b) Most often irritable.
(c) Sometimes pleasant.
(d) Most frequently pleasant.
(e) Always pleasant.

(2) Does he take part in *sensible* "back and forth" conversation, *listening* as well as *talking* to you, not just short answers to your questions, but a "give and take" conversation?

(a) Never "back and forth" conversation.
(b) Occasional "back and forth" conversation.
(c) Fairly often "give and take" conversation.
(d) Usually good "back and forth" talk.
(e) Almost always listens and talks realistically.

(3) Are the elements of his speech logically consistent and connected by some idea or relationship, or do they tend to be inconsistent and disconnected? Rate what is most representative during the interview.

(a) Coherent and consistent.
(b) Slightly incoherent and inconsistent.
(c) Distinctly incoherent and inconsistent.
(d) Conspicuously scattered, disconnected, or incoherent.

(4) Does he give evidence of: (a) Knowing who he is,
(b) Recognizing several persons about the hospital,
(c) Knowing the names of several persons around the hospital?
(a) Knows all three.
(b) Knows any two.
(c) Knows any one.
(d) Knows none.

An analysis of the initial ratings for each group reveals non-significant differences between groups prior to treatment.

Following the initial pre-experimental ratings, the period of treatment was begun. Ratings on each patient were then performed at weekly intervals for the following eight weeks, providing in all a total of nine weekly ratings for each patient. Weekly ratings two through five encompass the period of treatment. The final four ratings cover the four week post-experimental period during which all medication was again withheld.

Results

Weekly comparisons revealed no significant variations from the base line on blood pressure, complete blood count and urine examination for bilirubin, that is, no hypotension, leukopenia or jaundice was observed. Skin reactions or visual difficulties were not experienced. The only significant undesired side-effect was a single episode of spasmodic torticollis in one patient on the second day of treatment, three hours after she had received her third 16 mg. tablet. The patient (active treatment group) was taken off medication for 24 hours and then allowed to catch up without experiencing similar difficulty; however, this patient later developed marked extra-pyramidal signs that were allowed to go uncontrolled.

No member of either Group I or Group II developed Parkinson-like signs.

C-scale (Communication)

A comparison of pre-experimental and post-experimental ratings for all patients indicates significant differences (Sign Test

p .01). Differences of this magnitude in a group of 38 subjects would be expected as a result of chance fluctuations only once in 100 times. Closer examination of the data reveals the following: No significant change is found within Groups I, II or III. Significant change is observed only within Groups IV (Sign-Rank Test p=.05) and V (Sign-Rank Test p<.0005), both of these groups being treated with Trilafon only. The probability that the observed significant differences are the result of chance alone is then five times in 100 and fewer than five times in 10,000 respectively. The extra-pyramidal signs are apparently related to improved communication between these patients and the psychiatric staff. Significant changes in communication are not observed when extra-pyramidal effects are controlled with Cogentin. While desirable changes in communicative success are seemingly related to the presence of extra-pyramidal signs, even more dramatic changes occurred within the Trilafon treated group resistive to development of the signs.

K-scale (Conceptual Disorganization)

Pre-experimental and post-experimental ratings show lack of significant change within any of the groups. Interestingly, however, Group V was significantly different one week following cessation of treatment (Sign Test p=.02) but the difference fails to persist beyond this period. The findings are perhaps suggestive of improvement in conceptual organization while treated with Trilafon, but in no way support the contention of significant advantage associated with extra-pyramidal signs.

F-scale (Perceptual Distortion)

Changes within none of the groups approaches significance. Apparently, neither Trilafon alone nor Trilafon to the point of Parkinson-like signs was sufficient to meaningfully alter behavior on this dimension.

A-scale (Affect)

No significant changes are present between the pre-experimental and post-experimental ratings for any of the groups. Here again, neither Trilafon alone nor Parkinson-like signs induced by Trilafon was followed by meaningful changes in behavior.

Discussion

One of the more enthusiastic reports on the therapeutic efficacy of extra-pyramidal signs is the finding by Dixon[1] that following withdrawal of prochlorperazine, "the patients, almost a hundred per cent, went into remissions." Dixon used only 11 cases, of varied diagnosis, and apparently was able to induce the signs in all. The criteria used in selection and the eventual determination of remission are not clearly indicated. An observation common to both the Dixon study and the present investigation was the onset and permitted duration of the extra-pyramidal syndrome. Trilafon, used with a group of chronically psychotic women, resulted in Parkinson-like signs for 30% of the group with onset being 3 to 16 days after the initiation of treatment and requiring a dosage ranging from 48 to 128 mg. daily. Other reports on other phenothiazines with dissimilar groups cite the incidence as ranging from 18% to 88%. Weiss et al.,[5] have recently reported an incidence of 38% in using Trilafon with chronically psychotic women.

Brooks[2] has found, "that the therapeutic effects were not dependent on occurrence of extra-pyramidal dysfunction. On the contrary, alleviation of such dysfunction, as soon as it occurred sped the progress of recovery." The results of this study may be regarded as being at variance with the above finding. Group III, those patients who developed extra-pyramidal signs and received Cogentin as a control for the symptoms, clearly show no significant changes on any of the behavior scales and in this way were indistinguishable from the two placebo groups.

Summary and Conclusions

A ward of 38 chronic women patients was sorted at random into control and experimental groups in an attempt to study pharmacologically induced Parkinson-like signs as a therapeutic index. The five groups of patients were treated as follows. Group I (N=5) received a Trilafon placebo only; Group II (N=4) received Cogentin only; Groups III (N=5) and IV (N=5) were paired alternately in the order in which they developed extra-pyramidal signs, Group III receiving Cogentin as a control for the signs;

Group V (N=21) received Trilafon in rapidly increasing dosages up to 128 mg. daily without consequent Parkinson-like signs. The patients' behavior was scaled on the "affect" and "communication" scales of the MACC Behavioral Adjustment Scale (Ellsworth), and the "perceptual distortion" and "conceptual disorganization" scales of the Multidimensional Scale for Rating Psychiatric Patients (Lorr).

Each subject was rated weekly, the first rating taking place after a two week interval free from all medication. Treatment was then initiated and the subjects were rated each week for the ensuing eight week period, the first four weeks constituting the treatment period and the final four weeks comprising the post-experimental period during which time all medication was again withheld. Pre-experimental and post-experimental ratings were then compared for the presence of significant change in behavior.

Neither Group I, nor Group II developed extra-pyramidal signs. Group IV (extra-pyramidal signs without control), following withdrawal of medication, appears to have benefited significantly with respect to communicative success with others, but showed a lack of significant change on other behavior variables. Group III (extra-pyramidal signs with Cogentin), like the two placebo groups (I and II), showed no significant behavior change on any of the behavior variables rated. Group V, those patients receiving Trilafon but failing to develop Parkinson-like signs at any dosage, from 32 mg. daily to 128 mg. daily, showed an even more dramatic and persistent change in communicative success during the post-experimental period and a transient improvement in conceptual disorganization which dissipated rapidly during the post-experimental period.

The results clearly indicate some improvement following prolonged extra-pyramidal signs with equal or better effects attained by those patients receiving Trilafon but resistive to the signs. The presence of induced Parkinson-like signs may be suggestive of potential improvement but certainly is not unequivocally advantageous. It may well be that dosages short of extra-pyramidal effects could have produced equally effective or better outcomes in those patients who did develop signs.

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REFERENCES

1. Dixon, C. H.: Conference of Missouri Neuropsychiatric Hospitals Report on Prochlorperazine, July 1957.
2. Brooks, G. W.: *New Engl. J. Med.*, 254: 1119, June 1956.
3. Hall, R. A., Jackson, R. B., and Swain, J. M.: *J.A.M.A.*, 161: 215, May 1956.
4. Ayd, F. J.: *Dis. Nerv. System*, 18: 394, Oct. 1957.
5. Weiss, I. I., Rubinger, J. H., Sorin, M., and Ryzen, N.: *Am. J. Psychiat.*, 114: 1118, June 1958.

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Effects of Iproniazid on Chronic and Regressed Schizophrenics

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Iproniazid, marketed under the trade name of Marsilid by Hoffmann-La Roche, was developed several years ago as a chemotherapeutic agent for the treatment of tuberculosis. While more effective than the closely related isoniazid (Rimifon), it proved toxic when given in required therapeutic doses. Among the various side-effects, euphoria was observed in a good number of patients. This was even noticed when iproniazid was given in doses considered too small to be effective for the treatment of tuberculosis. Because of this euphorizing effect, it is now being used as an anti-depressant and stimulant in psychiatry.

Iproniazid is a monoamine oxidase inhibitor and as such exerts powerful pharmacological effects by delaying the inactivation of highly potent neurohormones such as serotonin, epinephrine and norepinephrine, all of which are monoamines and normally inactivated by monoamine oxidase. It is interesting to note that, while iproniazid leads to an increased serotonin level in the brain and euphoria, reserpine, widely used in psychiatry as a tranquilizing agent, reduces the serotonin level in brain tissue and is known to cause depression in many patients.

While the effect of iproniazid on the acutely depressed patient has been studied extensively, we were interested in its effect on chronic and regressed schizophrenics. For our study a group of 36 men and 28 women were selected and placed in respective wards. The youngest patient was 22, the oldest 61 years old. The mean age was 44 years; 54 patients, or 84%, were chronic schizophrenics, 16% had various other diagnoses such as mental deficiency with psychosis, manic depressive psychosis, and chronic brain syndrome. The duration of illness ranged from 2 to 37 years, with an average of close to 19 years. Only 2 patients had been ill for less than 5 years. Duration of illness was determined by the date of first hospitalization.

From New Jersey State Hospital, Trenton, N. J.

The patients were selected according to certain common characteristics. All were more or less apathetic and/or depressed, withdrawn, negativistic, careless and untidy. They were grouped into pairs by the following random method:

The patients of each group were arranged in two columns, one having odd, the other even last digits of hospital numbers. Each column started with the lowest and continued to the highest numerical value of the last digit. When this method did not divide the group evenly, the following digit of the hospital number was used for dividing the excess group, and so on until finally two columns containing an equal number of patients each were obtained. The corresponding members of each column were matched into pairs and the members of each pair compared to each other on a rating sheet as to which of the two showed more:

1) Apathy, withdrawal, listlessness.
2) Work ability and endurance.
3) Spontaneous talk and conversation.
4) Careless, untidy and sloppy habits.
5) Depression, restlessness and negativism.
6) Normal appetite, eating spontaneously without prompting or spoon feeding.
7) Poor sleep pattern.
8) Confusion, disorientation, strange or bizarre behavior.

Rating was done independently by three observers. The initial ratings were not accessible to the raters following completion of the sheets. Finally, a coin was tossed to decide which column of each group would receive the placebo and which the drug. The result was kept secret from the raters.

The dosage consisted of 50 mgm of either iproniazid or placebo orally three times daily for all patients throughout the experiment. The placebo used consisted of 50 mgm capsules of sugar and a small amount of riboflavin which gave it a yellowish appearance similar to that of the Marsilid tablets. Medication was continued for 8 weeks, at which

time the patients were re-rated by the same observers and method.

The above described method was chosen because of its relative objectivity and simplicity. In our patients, a decrease in depression was found in 6 patients, or approximately 20% of those receiving the active drug. None of the placebo patients showed improvement of depression. The chance probability of obtaining this result is less than .04. Otherwise the changes in ratings, although generally indicating some stimulative effect upon the iproniazid group, were not sufficiently prominent to be statistically significant.

In addition to the rating system described above, detailed and careful observations and records of clinical data were collected on the group of the 28 female patients. A comparison of the iproniazid treated group with the placebo group on the basis of these observations showed quite marked and interesting changes in the former which the rating sheet, by its design and limitations, failed to reflect.

The following is based on a careful analysis of reports, progress notes and observations of the female group only, but it is our impression that an equally detailed and careful observation of the male group would have resulted in similar findings.

1) While the control patients did not show any psychomotor changes, we saw six cases of increased psychomotor activity with agitation in the iproniazid group. This was persistent and lasted until the drug was discontinued. One of these patients became continuously sexually aggressive. One statuesque catatonic showed only increased tension and one emotional outburst without increased motor activity. One depressed patient showed improved mood and increased motor activity without agitation.

2) Twelve incidents of physical aggression involving iproniazid patients were reported in writing by the ward personnel during the two months treatment period. The actual number of these incidents was even greater because some of them were reported only verbally. No such incidents were observed with the control group.

3) Four patients of the iproniazid group said they "felt better," and two complained of feeling irritable. Irritability was observed by us in at least three more patients of this group. No patient of the control group made similar statements and no signs of increased irritability were observed.

4) Reactivation of psychosis was not observed in any of the control patients, but three of the iproniazid patients became actively hallucinated although they had not shown signs of hallucination for considerable time prior to the experiment. Two of these developed short lasting stuporous states under minor physical stress, represented by indigestion in one case and incision of an infected finger in the other.

5) Signs of behavioral improvement were seen in two patients on placebo and nine of the iproniazid group. They became more alert, and were in better contact. In three instances, however, this behavioral improvement was accompanied by a marked degree of agitation and weight loss.

6) Side reactions described in the literature, such as jaundice, constipation, neurological signs, edema or skin reactions were not observed in our series. There were no signs indicating marked blood pressure changes, such as fainting or dizzy spells, and no complaints about blurred vision or tinnitus. We saw a persistent flushing of the face in only three cases in the iproniazid group. The absence of subjective side effects can perhaps be explained with the type of the selected patients. They were more or less regressed and indifferent individuals who had little inclination to complain or communicate.

7) The follow-up of the patient's weight resulted in interesting findings. While there was an average gain of 5.2 pounds of the 14 female patients receiving the drug over the 8 weeks period, the individual weight changes were quite remarkable. One patient gained 25, two 16, one 13 and two 11 pounds. On the other hand, there were individual losses of 13, 10, 6 and 4 pounds. The 14 female patients on placebo showed an average gain of 3.5 pounds, but individual changes were much less pronounced and in only two patients amounted to more than 4 pounds.

According to the literature a weight increase has to be expected with iproniazid medication. Our findings show that this is not always so. It might be more consistently

true in actively depressed patients where the removal of depression leads to the removal of a psychogenic anorexia and therefore to an increase in weight. In our observation all those patients lost weight on iproniazid who responded to the drug with more or less marked agitation and tension.

Summary and Conclusion

Iproniazid was given for 8 weeks in doses of 150 mgm daily to 32 chronically ill, withdrawn, apathetic and depressed mental patients of both sexes, mostly schizophrenics. An equal number of controls received a placebo. Strict randomization and double blind procedures were followed. Results obtained by a rating sheet showed that 20% of the 32 patients treated had shown improvement as to apathy and/or depression. Additional information was obtained from close clinical observation of the group of 14 female patients and their controls included in this study. These results can be summarized as follows:

1) The drug improved alertness, contact, and spontaneity in more than 50% of patients, and at the same time caused undue agitation in a considerable number, rendering them more aggressive, tense and irritable, and increasing their psychomotor activity.

2) Marked individual weight changes were noticed ranging from a gain of 25 pounds to a loss of 13 pounds. Weight loss occurred in those who displayed tension and agitation under the influence of the drug.

3) Reactivation of psychotic patterns was observed in a small but significant number of patients. No side reactions in the somatic area were observed.

Iproniazid in doses of 150 mgm daily has a marked effect on a considerable number of chronically ill mental patients. The nature of this effect is complex, but therapeutically promising and requires further investigation.

REFERENCES

"Marsilid" (iproniazid), Abstracts of papers presented at *First Marsilid Symposium,* New York City, No. 29-30, 1957.

Loomer, H. P., Saunders, J. D., and Kline, N. S.: Iproniazid, An Amine Oxidase Inhibitor, As an Example of a Psychic Energizer. *Reported read at Regional Research Conference of the American Psychiat. Assn.,* Syracuse, N. Y., April 6, 1957.

Udenfriend, S., Weissbach, H., and Bogdanski, D. F.: Effect of Iproniazid on Serotonin Metabolism in Vivo. *J. Pharmacol. & Exper. Therap.,* 120:255-260, June, 1957.

Saunders, J. C., Radiger, N., and Kline, N. S. L.: A Theoretical and Clinical Approach to Treating Depressed and Regressed Patients with Iproniazid. *Report read at 12th Annual Convention of Society of Biological Psychiatry,* Atlantic City, N. J., June 15-16, 1957.

Crane, G. E.: Further Studies on Iproniazid. *J. Nerv. & Ment. Dis.,* 124:322, Sept. 1956.

Nussbaum, H. D., Leö, W., Mattia, V. D., Jr., and Hillman, E.: The Eöects of Iproniazid Phosphate (Marsilid) on Hypertension (Preliminary Report). *Angiology* 8, No. 2, 198-200, April, 1957.

Robie, T. R.: Marsilid and Electroconvulsive Shock Therapy. *J. Clin. & Eper. Psychopathol.,* 19: 90-97, Suppl. 1, June 1958.

————: The Use of Iproniazid in Psychiatric Patients. *Medical Science,* 1:41-44, April 10, 1957.

————: Serotonin. *Ann. Int. Med.,* 46:425-430, Feb. 1957.

Kamman, G. R., Freeman, J. G., and Lucero, R. J.: The Eöect of 1-Isonicotinyl 2-Isopropyl Hydrazine (IIH) on the Behavior of Long-Term Mental Patients. *J. Nerv. & Ment. Dis.,* 118:391-407, 1953.

Alexander, L.: Chemotherapy of Depression. *J.A. M.A.,* 166, No. 9, 1019-1023, March 1, 1958.

Ayd, F. J., Jr.: A Preliminary Report on Marsilid. *Am. J. Psychiat.,* 114, No. 5, 459, Nov. 1957.

Ferreira, A. J. DeL., and Freeman, H.: A Clinical Trial of Marsilid in Psychotic Depressed Patients. *Am. J. Psychiat.,* 144, No. 10, 933-934, April 1958.

Robie, T. R.: Marsilid in Depression. *Am. J. Psychiat.,* 144, No. 10, 936-937, April 1958.

Use of Hydroxyzine in Psychosis

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This paper is a report of the clinical reaction of hydroxyzine (Atarax) in a group of 17 chronic male psychotic patients. These patients were studied from two points of view, the clinical behavioral effect and the laboratory effect.

Atarax as a chemical compound is designated generically as hydroxyzine and chemically as 1-(p-chlorbenz hydril)-4-[2-2(hydroxyethoxy) ethyl] diethylenediamine. Because this compound is readily soluble in water, it is rapidly absorbed in the gastrointestinal tract and reacts quickly.

Method:

This study of 17 chronic psychotic patients was started in November 1956 and continued for a six month period. All the patients were privileged and resided on an open ward in a psychiatric hospital. For one reason or another they did not seem to show any progress on the treatment they had been receiving over a period of years, but remained on an open ward because they were capable of handling themselves while in the hospital environment. Since there was little known about hydroxyzine it was decided to study laboratory effects on the patients. With this in mind, liver function tests, urine analysis and blood counts were taken at the beginning of the study prior to administering hydroxyzine and at various times during and at the termination of the study. The 17 patients selected had had other tranquilizing medication and other types of treatment previously. The group consisted of three catatonic, four paranoid, three hebephrenic, three undifferentiated and two simple types of schizophrenics, and two manic depressive psychotics, manic types. The length of stay in the hospital ranged from two to 12 years and their ages ranged from 27 to 50 years.

In order to study the clinical behavioral effect of the medication, the writer, who knew the patients for at least two years, decided to evaluate each patient on the basis of ten behavioral trait groupings. Each patient was evaluated prior to medication and during the period of six months. Changes were noted from day to day and then the patients were re-evaluated at the end of six months.

Four basic symbols were used to indicate the presence or absence of the behavioral trait grouping as is shown in Chart I. C designates constant presence of the behavioral trait; F indicates frequent presence of the trait; O was occasional presence and N that the trait was absent. There were some traits that were not clearly in evidence and therefore a single symbol could not be used. Here a double symbol was used such as F-C.

Results:

The evaluation indicates that in some categories there was more improvement shown than in others. The largest number of characteristic behavioral traits for the 17 cases was in the behavioral trait grouping which was overwhelming fear and anxiety or tension. Here there were 14 patients of the 17 that had clinical evidence of these traits. Two had them constantly, one from frequently to constantly, seven frequently and four occasionally. After receiving hydroxyzine for six months there was an outsanding improvement noted on evaluating this grouping. There were seven patients who had these symptoms occasionally, three frequently, one frequent to constant and three became free of these symptoms.

The next most frequent symptomatology was found in the symptom group which consisted of bizarre behavior, autistic or delusional thinking. Here 13 patients showed symptoms. Eight were frequent and five occasionally. Here evaluation showed five occasional, two frequent, one frequent to occasional and five lost the symptoms altogether. In this category we also see an outstanding improvement.

One other category which was noteworthy in the improvement shown was in the area of confusion and disorientation. Here eleven patients had these traits. Seven were occasional, three frequent and one constantly. On evaluation it was found that two had the symptoms constantly, three occasionally and six had lost these symptoms completely.

There were eleven patients who had incapacitating compulsions or obsessions. Six were frequent, three constant and two occasional. On evaluation three were frequent, five were occasional, two were occasional to non-existent and one had lost this symptomatology. Here also the improvement was impressive.

Nine patients had perceptual disturbances and hallucinations. Two had them frequently. The result here was also quite impressive when evaluation was completed. Three patients had the symptoms occasionally, one frequently and five had lost these symptoms.

There were six patients with severe depressions or guilt symptoms, which were a characteristic of the majority of these patients; three of them occasionally, and three frequently. This changed to one frequently, one frequently to occasionally and four lost these symptoms.

Six patients showed catatonic behavior. One frequently, one constantly, and four occasionally. This changed to one patient remaining constantly catatonic, one occasional to non-existent and in four patients this symptomatology had disappeared.

Five patients had the symptoms of assaultiveness occasionally. All these patients lost their assaultiveness.

Four patients provoked assaults from others. Two of them frequently and two occasionally. Here it was found that three did this occasionally and one lost this behavior trait when they were evaluated.

In the last category, overt sexual deviations, there were two patients who showed these symptoms frequently. Evaluation found that one changed to having the trait occasionally and one patient lost this trait.

This evaluation shows that hydroxyzine has produced improvement in the behavioral traits evaluated. In some categories this improvement was impressive.

The dosage of hydroxyzine used was from 59 mg. three times a day to 100 mg. three times a day with the average and optimum dosage being 75 mg. three times a day.

Liver function tests were performed prior to taking hydroxyzine and six months after taking the medicament for this period. The tests chosen were serum bilirubin, cephalin flocculation and thymol turbidity and after six months' use of hydroxyzine there were no changes in the liver functions.

Complete blood counts were made before and after the use of hydroxyzine. After six months' use of this medication there were no blood dyscrasias. Some patients were taken off the medication because improvement was not maintained over a long enough period and a new medicament was instituted.

Case Histories

Case 1: Hydroxyzine increased slowly to 50 mg. TID. Prior to hydroxyzine he was tremulous, exceptionally compulsive, had overwhelming fear, depression, delusional thinking, rigidity in purpose and desires. After hydroxyzine therapy patient seemed more alert, less fearful, tremulousness decreased, listened to reason and had a lessening of his rigidity and compulsiveness. However, the immediate change did not last and the over-all picture showed slight improvement.

Case 2: A schizophrenic paranoid type. Prior to hydroxyzine patient showed psychomotor retardation, was withdrawn, underproductive, rigid facial expression, occasional somatic complaints which were increasing with his delusional thinking and bizarre behavior and autistic ruminations. He was placed on hydroxyzine therapy 50 mg. TID. He improved to some extent in his behavior. He showed more interest in his environment and became a little more productive. Somatic complaints decreased. However, because it was felt that the improvement was not sufficient in this case, the drug was discontinued after seven months.

Case 3: Prior to hydroxyzine patient was very insecure, showed poor judgment, was fearful and tense. After hydroxyzine, gradually increased to 100 mg. TID, he seemed to show better judgment, is brighter, less fearful and rarely showed tension. However, patient showed much aggressiveness. He became involved in an altercation and was transferred out of the ward.

Case 4: Hydroxyzine medication gradually increased to 50 mg. TID. Prior to hydroxyzine patient was slovenly. He had many somatic complaints, always felt sleepy. His affect was inappropriate. He was deteriorating and withdrawing. After hydroxyzine patient became brighter, showed ambition, appeared much neater, affect was more appropriate. His interpersonal relationships were better. Patient was placed on trial visit and after six months was discharged from the hospital.

Case 5: Hydroxyzine gradually increased to 75 mg. TID. This case improved with hydroxyzine in that his affect was more appropriate and he seemed brighter and became more independent. However, because his improvement was not maintained, medication was discontinued.

Case 6: Hydroxyzine gradually increased to 100 mg. TID. This patient had exhibited himself and masturbated in public frequently. He was tremulous, fearful, manneristic and dependent. After hydroxyzine he became more independent. His tremors decreased and he became much less manneristic. He stopped exhibiting himself and masturbating. In this case it was decided to try another tranquilizer to see if the patient could become more interested in leaving the hospital. Within a few days his old symptoms reappeared and within a week he was regressed. Hydroxyzine was reinstituted and the other medication discontinued and within two days improvement was clearly noticed. Patient maintains his improvement and seems satisfied with the hospital environment.

Case 7: Hydroxyzine was gradually increased to 100 mg. TID. Prior to hydroxyzine patient was very aggressive and had homocidal tendencies. He hallucinated, was delusional, was passively cooperative and rather inappropriate. He was asocial and spoke very little. His psychomotor activity was retarded and he showed no interest in his surroundings. After hydroxyzine started patient began to brighten up, eyes appeared brighter, smiled appropriately, conversation became relevant and he showed good spontaneity. He became neat in appearance and attended and participated in all social functions. For a time, after a high dose of medicine, patient complained of pain that would last from five to ten minutes. After lowering dosage this disappeared and did not return again even though medication was increased. Patient left hospital on trial visit.

Case 8: This case showed little change on hydroxyzine although he did become somewhat brighter but because of his underlying personality structure, medication was discontinued.

Case 9: This patient had hydroxyzine up to 100 mg. TID and although medication reduced the amount of fear and anxiety and the patient seemed brighter, it was felt that his improvement was not maintained well enough and therefore this medication was discontinued.

Case 10: Hydroxyzine was gradually increased to 100 mg. TID. Before hydroxyzine this patient was frequently abusive. He felt he was being discriminated against and was grandiose in trying to bribe personnel to allow him to leave the hospital. After hydroxyzine he was much brighter, more cheerful. Outbursts of anger and verbal abusiveness became infrequent. He was more cooperative and friendly and has been permitted to leave the hospital on passes in his own custody.

Case 11: In this case hydroxyzine did not seem to have too much effect although patient was easier to handle. Medication was discontinued.

Case 12: Hydroxyzine gradually increased to 100 mg. TID and then reduced to 75 mg. TID. Although hydroxyzine seemed to cause a change in this patient's attitude, in that he brightened up, became more friendly, socialized more and showed more interest in his environment, progress did not seem

CHART #1

		Catatonic	Paranoid	Paranoid & Convulsive Disorder	Hebephrenic	Catatonic	Paranoid	Hebephrenic	Undifferentiated & Transvestism	Manic Depressive, Manic	Paranoid	Hebephrenic	Undifferentiated	Simple	Catatonic	Undifferentiated	Manic Depressive, Manic	Simple
		1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17
Severe Depression and/or	P	O	N	O	O	N	N	N	F	N	N	N	N	F	N	N	N	F
Guilt	A	N	N	N	N	N	N	N	N	N	N	N	N	F-O	N	N	N	F
Assaultiveness	P	N	N	N	O	N	O	O	N	N	O	N	N	N	N	O	N	N
	A	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Provokes Assaults from Others	P	N	N	N	N	N	F	N	N	N	O	N	N	N	N	F	N	O
	A	N	N	N	N	N	O	N	N	N	N	N	N	N	N	O	N	O
Catatonic Behavior	P	N	N	N	N	N	F	O	O	O	N	N	N	O	C	N	N	N
	A	N	N	N	N	O	N	N	N	N	N	N	O-N	N	C	N	N	N
Incapacitating Compulsion or	P	C	N	N	N	N	F	N	F	O	F	O	F	C	C	N	F	F
Obsession	A	O	N	N	N	N	O	N	O	O	O	O-N	O-N	F	C	N	F	F
Overwhelming Fear, Anxiety	P	C	N	F-C	O	O	F	N	F	O	O	F	N	C	F	F	F	F
or Tension	A	O	N	O	O	N	O	N	N	O	N	O	N	F-C	F	O	F	F
Perceptual Disturbances and	P	F	N	O	O	N	N	O	N	N	C	N	O	N	O	N	O	F
Hallucinations	A	N	N	N	N	N	N	N	N	N	O	N	N	N	O	N	O	F
Bizarre, Autistic, or Delusional	P	F	O	O	F	N	O	O	N	N	F	F	F	F	O	N	F	F
Thinking	A	O	O	N	N	N	N	N	N	N	O	O	N	F-C	O	N	F	F
Disoriented, Confused	P	N	O	N	N	N	N	N	N	N	N	N	N	O	O	N	F	F
	A	N	O	N	N	N	N	N	N	N	N	N	N	O	O	N	F	F
Overt Sexual Deviations	P	N	N	N	N	N	N	N	O	N	N	N	N	N	N	N	N	N
	A	N	N	N	N	N	N	N	O	N	N	N	N	N	N	N	N	N

P—Prior to Atarax Medication
A—After 6 mos. on Atarax

O—Occasional
N—Not Present

C—Constant
F—Frequent

to be maintained after several months and the medication was discontinued.

Case 13: In this case hydroxyzine did not seem to have any great effect and therefore medication was discontinued after six months.

Case 14: There is very little change in this patient's condition with hydroxyzine therefore the medication was discontinued after six months.

Case 15: Hydroxyzine was gradually increased to 100 mg. TID. Prior to use of the drug this patient was noisy, was an agitator, cursed and swore and was always getting into some difficulty. After hydroxyzine patient showed improvement, he became friendly, pleasant and much easier to handle, works around the building and does not annoy the other patients any more.

Case 16: Hydroxyzine was gradually increased to 100 mg. TID and patient showed improvement for awhile but when somatic conditions returned, medication was discontinued.

Case 17: At first hydroxyzine seemed to improve this patient but because progress was not maintained the medication was discontinued after a six months' trial.

Discussion:

The effect hydroxyzine had on this group of chronic psychotic patients was encouraging. There were no symptoms referable to abnormal changes in the liver function tests after six months of the medication. There were no blood dyscrasias noted and there was very little change in the blood counts. As far as liver function and blood counts are concerned hydroxyzine is shown to be a safe medication. One patient complained of pain in chest on 100 mg. dose TID, but on lowering dosage this disappeared and did not appear again after increasing the dosage.

One patient had a return of symptoms within a week after the medication was discontinued but on prescribing hydroxyzine again the symptoms disappeared. For the period of six months there were no other abnormal side effects. From the clinical behavioral effect this medication has shown good results especially in the specific behavioral symptoms. Improvement of symptom complexes, including overwhelming fear, anxiety or tension demonstrates that hydroxyzine is a good choice for use in this area. It has shown good results in bizarre, autistic or delusional thinking. The results in all the other behavioral traits seemed impressive. In specific type of psychosis, improvement was not impressive because of the complexities of the symptomatology; as described above, certain behavioral traits reacted favorably to the hydroxyzine. In those cases where the medication was discontinued there seems to be grounds for further investigation to determine why the initial improvement was not maintained.

The over-all picture was encouraging because of the improvement in some of the behavioral traits in several of the cases. Medication was discontinued in some cases because of other severe personality defects and severe symptomatology.

Summary:

In summary, hydroxyzine was used in 17 cases which were studied closely over a period of six months. Generally, all patients became more interested in their surroundings and became more alert. The drug is considered safe since no side effects, blood dyscrasias or dysfunction of the liver were encountered. Certain symptom complexes were rated and described in the paper. Hydroxyzine was exceptionally beneficial in alleviating the symptom complexes consisting of overwhelming fear, anxiety or tension and the symptoms of bizarre, autistic or delusional thinking.

In this study, one patient was discharged, one was placed on trial visit and three patients showed continued improvement. One of the improved patients had his medication discontinued and within one week had a return of symptoms. When hydroxyzine was re-prescribed, the symptoms disappeared.

Hydroxyzine has been shown to have a definite place in the treatment of psychotic patients since all these patients had been tried on other tranquilizers and other forms of treatment.

The improvement noted and the results reported have continued to date.

BIBLIOGRAPHY

Farah, L.: Preliminary Study on the Use of Hydroxine in Psychosomatic Affections. Jalisio, Mexico.

Steroid Therapy Adjuvant to Psychotherapy of Childhood Ulcerative Colitis

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Although ulcerative colitis ordinarily begins in adult life,[9] it is by no means unusual in children.[2,3] Between 10 and 11 per cent of all reported cases have their onset before the age of fifteen, with the commonest age in childhood being 8.5 years. Such leading gastroenterologists as Bockus[3] and Bargen[1] feel that any type of treatment is less effective with children than with adults, and many express doubt that psychotherapy has any particular effect on the course of the disease. The literature is full of conflicting reports indicating that sulfa drugs, steroids, and psychotherapy are each the preferred treatment of a substantial group of equally distinguished internists.

The effectiveness of psychotherapy would certainly be difficult to assess in any small group of patients, since the natural course of the illness is so variable.[5,7] The majority of child and adult patients have chronic intermittent colitis, averaging one serious attack every other year, alternating with complete remissions which may last for several years. Of 134 children studied in Sweden,[11] 108 or 78.8 per cent had chronic intermittent colitis for ten years of follow-up. Of the remainder, 1.5 per cent died of fulminating disease within one year, 12.4 per cent had chronic continuous colitis, and 7 per cent had a single attack followed by a minimum of six years freedom from illness at the time of the report.

Thus, it is apparent that any therapeutic approach may give rise to false optimism, for the child may be one of the few who never has a second attack, or one of the vast majority who have long remissions between attacks. With this sobering fact in mind, the present discussion will focus on a combined medical-psychotherapeutic approach, in which steroids induce remission of active colitis and help maintain it while psychotherapy is in progress.

Presented at the thirty-third annual convention of the Central Neuropsychiatric Association, Dallas, Texas, October 18-19, 1957.

In the cases to be discussed, the referring pediatricians intended quite simply to use every conservative tool at their command, with no thought of facilitating psychotherapy by the administration of steroids. They were acting on the basis of a large body of literature published since 1950, which indicates that ACTH, Cortisone, and related compounds induce rapid clinical remission in about 75 per cent of colitis cases.[16,17,20] Most of these papers have a sentence tucked in near the end recommending that psychotherapy should accompany steroid therapy, but very little has been published from the psychotherapist's point of view. Paulley[14] has mentioned using ACTH as an adjuvant to psychotherapy in two cases of a 43 patient series, the remainder of whom received psychotherapy alone; and Saver[18] et al., have described the psychotherapeutic use of ACTH in one adult patient who was taught to give herself the hormone at stressful times. Theodore Lidz, in discussing this case, commented that the introduction of steroids has made the psychotherapy of ulcerative colitis much easier. This point is stressed in the following brief case reports.

Three children suffering from ulcerative colitis were admitted to the pediatric service of the John Sealy Hospital during 1956. One set of parents refused to allow psychiatric consultation. The other two children and their parents cooperated in daily intensive work during hospitalization, and have been seen intermittently at intervals of two weeks to three months ever since. Both families live several hundred miles from Galveston, in small communities where no psychiatrist is available.

It will be noted that both children have the usually reported conforming, passive, obsessive, outwardly well-adjusted character structure common to most such patients. The parents, too, have the type of psychopathology and relationship with each other so well described by Engel,[6] Mohr,[13] and others[8,12,15,19] This is mentioned simply to point

up that these two families are typical of most cases of childhood ulcerative colitis, in family structure, precipitating situation, and age of onset.

Case No. 1 is Virginia M., aged 9 years 9 months on admission in August 1956. She had had diarrhea continuously since May 1955, when her parents and others in the community had all suffered an attack of "intestinal flu." Although afebrile, she had continuous diarrhea for 15 months. She had to carry a potty in the family car to avoid accidents, and stopped riding her bicycle for the same reason. Never a hearty eater, she had severe anorexia, and was markedly underweight and pale. The parents knew of no special stress, and felt that she had always been a satisfactory child.

Virginia is an only child, her mother having had two miscarriages previously. Mrs. M. is Rh negative, and became sensitized during the first two pregnancies. Because of this, Virginia's birth was one month early after an induced labor. Although she did not have erythroblastosis, the parents were advised not to have any more children. She developed rapidly and normally, being an excellent student, very obedient, and "good." Except for failure to eat all of the balanced diet her mother felt she must have, there had been no known problems. Both parents emphasized proudly that they had a very calm home, that none of them ever raised a voice in anger or even irritation, and that no strong emotions were expressed at all. The father works for an oil company at a rather routine job; he had begun attending college at night during the year before Virginia became ill, because finances had prevented his doing so earlier. Furthermore, his wife was at the same time working on her master's degree in education at night and on Saturdays. He is naturally a fairly enthusiastic person, but had refrained from being demonstrative with Virginia partly because his wife did not approve and partly out of a personal conviction that his mother had "spoiled" one of his siblings and thereby caused him to become alcoholic. He felt his wife knew much more about raising children than he did because she is a school teacher and has college degrees, but occasionally he would take Virginia to the movies or on trips where he was more lenient with her than in his wife's presence.

Mrs. M. had had a very unhappy childhood, her mother having died in childbirth when she was about three. She spoke only German at that time, and was suddenly transplanted from her father's farm to her grandparents' home in town where she had to learn English. When she was five her father remarried and she looked forward happily to living again on the farm with a mother. To her dismay, the stepmother turned out to be an inconsistent, humorless individual who permitted an activity one day and punished severely for the same thing the next. Her father demanded and received scholastic excellence from all his children. She recalled his scolding her once because she had only the third highest grade average in school, whereupon she managed to pull up to number one. She early learned to keep her feelings to herself and to concentrate on good pergormance as the only path to peace. She has been a school teacher ever since her college graduation except for the first six years of Virginia's life. When questioned about her reaction to the advice that she have no more children, she replied that it was the only occasion in her adult life when she could remember having wept, and had hastily dried these tears as being a sign of weakness.

Virginia's first four hospital days were occupied with sigmoidoscopy, barium enema, duodenal intubation, and other uncomfortable diagnostic procedures. The child lay wanly in bed, counting her bowel movements and describing them in detail to the nurses. She did not talk to the other children, but lay quietly listening while her mother read to her. She cooperated with everything that was proposed in a rational, super-adult uncomplaining manner. Psychological testing revealed that she was functioning with an I.Q. of 133 and was highly critical of her own intellectual performance. Projective tests indicated that she regarded intelligence and self-control as the key to dominance; she felt her mother was the most intelligent and therefore dominant member of the family. She seemed overconcerned with controlling aggression and had some understandable anatomical preoccupation.

Meticorten was begun on the fifth hospital day. Within three days the stools decreased in frequency and improved in form, the anorexia disappeared, and she felt well enough to get out of bed. Within a week she was able to eat a regular diet and consumed it voraciously. Psychotherapy, begun at the same time as the steroid therapy, was at first entirely verbal despite the fact that it took place in a play room. Not for five months did she actually play in the therapy sessions. During the first few days of hospitalization she talked sweetly and obediently, indicating that everything at home was ideal. As the diarrhea subsided, she abruptly poured out a deluge of phobic and hostile material about her mother, her piano teacher, and school teachers she knew who were mean to dumb or handicapped children. To a lesser degree she objected to hospital rules and food, my being late for appointments, etc. She was especially disturbed by a long-standing fantasy that if she were bad, her mother might chain her to the wall and whip her; she had never been spanked or threatened with it since she had never misbehaved. After obtaining my promise not to tell her mother of this fear, she left the playroom at the end of the hour and told her mother herself. Mrs. M. was horrified to find out how Virginia felt, and wept freely as she talked with me later that day, realizing for the first time what an impossible example of controlled perfection she had been setting the child. Each day brought new material indicating Virginia's fear of failing at anything, fear of displeasing any adult, and fear of growing up and having to get two degrees. It is

difficult to convey with what minimal anxiety she was able to relate these things. The mother began to work through a delayed grief reaction over her own mother's death, and the father delightedly decided he should have trusted his spontaneous feelings all along instead of following his wife's over-intellectual lead. They left Galveston after four weeks, with Virginia in remission, taking 20 mg. of Meticorten daily.

All went well for several months, despite the mother's initial surprise at Virginia's new found ability to lose her temper and even greater surprise that the child could eat so much popcorn and candy without getting sick. The Meticorten dosage was gradually reduced during the fall and winter, until the first of May, when she abruptly developed severe colitis again. The precipitating situation was due to her superior performance in a piano recital with other grade school pupils. Her teacher then directed her to prepare five new pieces within two weeks and play in a recital for advanced high school pupils. After one week of effort, she had to be hospitalized in her home town, having up to forty stools daily. Virginia later told me that she had forgotten that she could complain to her parents about the teacher's demands, or refuse to appear. To quote her, "It's just this year I could tell them I was afraid of anything or didn't want to do something, and I forgot I could. I thought I was trapped and I really wasn't. I won't forget again."

Retesting by the psychology department in June, 1957 indicates that she now has a functioning I.Q. of 153, is more spontaneous and less self critical, and is effecting a far more favorable and affectionate attachment with her mother. She still is a very proper little girl, and hostility poses something of a problem for her, but she ordinarily expresses herself freely in all areas at the present time. She summed up her own appreciation of her changed situation in discussing her piano teacher: "I think I used to practice so hard just so I'd play well and everybody would say 'Oh, how good that teacher is! Now I'm just going to play the piano for me, and if she doesn't like it, I'll change teachers."

Case No. 2, Martha D., is a slightly younger child, eight years old at the time of admission in July 1956. She is the third of three daughters, her father being principal of the town's only elementary school, and her mother a teacher in the same school. She had her first attack of diarrhea in December 1954, at a time when she was supposed to appear in a school play. The onset was during the dress rehearsal, and so sudden that she soiled her clothing. It continued unabated until April 1955 when the parents withdrew her from school. They rehired a motherly housekeeper who had looked after Martha during her pre-school years, whereupon she promptly recovered. She remained well until December of 1955, when she was again involved in a program requiring costume fittings, rehearsals, and the necessity of performing before the whole school; the second attack began exactly as the first. Various local doctors were consulted to no avail, and in June 1956 she was referred to a pediatrician in a nearby city. He made the diagnosis of ulcerative colitis, started the child on meticorten, and advised the parents to bring her to Galveston for joint psychiatric-pediatric attention. Physically, she was well into a remission of her colitis on arrival, but was an extremely proper, over-sweet, dependent little girl. Psychometrics indicated she had an I.Q. of 114 and was a passive, compliant, obsessive child with a tremendous fear of growing up. This is not hard to understand in view of the fact that her mother is a driving, rigid individual who works continually at school and home, never seems to enjoy anything, and always worries. The mother attributed Martha's diarrhea to the fact that several people on the father's side of the family had intestinal disorders, and was puzzled at the notion that emotional factors might play a part in producing the illness. She readily agreed that she herself was chronically tense, depressed, and tired. Her own father had had multiple sclerosis throughout her childhood, and her mother had had to look after him while supporting a large number of children. She said she never got the idea from her mother that marriage or motherhood might be fun. Her mother had strict rules, such as that "everyone had to eat everything on their plates, and that's the way I run my house. My husband disagrees—there are lots of foods he doesn't like. He's always giving in to them about that, and bedtimes and privileges. He was raised differently —more easygoing." She added that he had tried to go into business once and failed, then returned to education, but he had never worried about the debts as she had.

The father, a pleasant individual, tried initially to relate as a co-expert by telling of his reading in psychology textbooks; he placed the onus of the problem at his wife's door. It was obvious that her cheerless, martyred rigidity was a factor, but his passive, almost sly conniving with the children to outwit their mother without overtly standing up to her was hardly helpful. He dwelt at great length on the happy times he and Martha had had before his business failed; then his wife and two older children were at school and he could come home to eat lunch with Martha and take her with him for several hours. Martha recalled the same pre-school period as almost heavenly, with only her daddy and the housekeeper around.

Despite the fact that the mother was anxious to become comfortable with herself and her family, her identification with her own mother was strong, and she had very mixed feelings about relaxing any of her household rules. She was able to accept Martha's feelings about her, which were expressed very freely during the steroid-induced euphoria, but kept wishing for the time when the medication could be reduced so Martha could "calm down again." She looked so fatigued and pale that I asked her when she had had her last medical checkup, to which she replied that she had had menstrual flooding for ten years, knew she was anemic, but did not

want to go to the expense of medical attention for herself. She felt she should "drag on." After six months, I finally persuaded her to consult a gynecologist, at which time her hemoglobin was only six grams per cent. For the first time in their married life, her husband asserted himself and insisted she go through with the blood transfusions and hysterectomy she needed. She seemed to enjoy his concern and forcefulness, but had trouble giving in gracefully.

Martha's own psychotherapy proceeded easily and rapidly, as she turned into a veritable chatterbox, relating meaningful fantasies, dreams and facts with equal lack of anxiety. During the first few months she began for the first time to play with children other than her sisters, to go out for the weekend, and to be more aggressive at home. She suffered one recurrence of colitis along with measles in the Spring but recovered rapidly. Repeat psychometrics after one year of therapy indicated her actual I.Q. to be 134 with evidence of considerable maturation and increased spontaneity in her relationships with her family. Despite great psychic improvement, she still has several loose stools a day and is still on maintenance steroid therapy.

Both these children were in the hospital for only one month. They were able to express their fears and angers as soon as the meticorten took effect. At no time did the colitis become worse as a result of becoming aware of, or expressing their feelings. Meticorten has been given for over a year, in ever smaller doses, largely to solidify psychotherapeutic gains before it is discontinued. Both of them have developed into leaders in their groups. Although both clinically and psychometrically tremendous improvement is evident, no predictions can be made as to the future course of their disease.

Engel, in his careful "Studies in Ulcerative Colitis," has delineated, not only the psychological factors which regularly appear in patients and families with this disease, but also points out physical factors which may precipitate attacks. Thus, in addition to the real or symbolic loss of the patient's key relationship, or any situation in which the patient feels helpless, attacks may also be precipitated by gastrointestinal infections, measles, or any upper respiratory infection. Psychotherapy, if successful, will render it unnecessary for the child to live only through compliance with the mother's wishes, and make normal ego growth more possible. It could hardly alter the basic propensities of anyone's colon, or prevent measles and influenza.

In the two cases presented, rapid strides were made in psychotherapy and in testing out new modes of interaction with parents and others. This would have been very difficult for these two obsessive, anxious, well-behaved little girls without the additional stress-resistance they gained from their steroid therapy.

Summary

The combined steroid-psychotherapeutic approach to ulcerative colitis in children offers possibilities for rapid intensive work with minimal danger of physical relapse. Continuation of maintenance steroid therapy over a prolonged period allows the child to test out new modes of social interaction wthout undue anxiety. The steroids can be gradually reduced and then discontinued once the therapeutic gains can be solidified by repeated succesful experiences.

BIBLIOGRAPHY

1. Bargen, J. A., and Kennedy, R. L. J.: Chronic Ulcerative Colitis in Children. *Post Grad. Med.*, 17: 27, Feb. 1955.
2. Bargen, J. A.: Complications and Problems Associated with the Management of Ulcerative Colitis. *Gastroenterologia*, 86: 674, 1956.
3. Bockus, H. L., Roth, J. L. A., Buchman, E., Kalser, M., Staub, W. R., Finkelstein, A., and Valdes-Dapena, A.: Life History of Non-Specific Ulcerative Colitis: Relation of Prognosis to Anatomical and Clinical Varieties. *Gastroenterologia*, 86: 549, 1956.
4. Clark, L. D.: Psychotherapy of Ulcerative Colitis. *Dis. Nerv. Syst.*, 17: 149, May 1956.
5. Cullinan, E. R., and MacDougall, I. P.: The Natural History of Ulcerative Colitis. *Gastroenterologia*, 86: 582, 1956.
6. Engel, G. L.: Studies of Ulcerative Colitis. I. Clinical Data Bearing on the nature of the Somatic Processes. *Psychosom. Med.*, 16: 496, 1954; Engel, G. L.: Studies of Ulcerative Colitis. II. The Nature of the Somatic Processes and the Adequacy of Psychosomatic Hypotheses. *Am. J. Med.*, 16: 416, 1954; Engel, G. L.: Studies of Ulcerative Colitis. III. The Nature of the Psychologic Processes. *Am. J. Med.*, 19: 231, Aug. 1955.
7. Flood, C. A., Lepore, M. L., Hiatt, R. B., and Karush, A.: Prognosis in Chronic Ulcerative Colitis. *J. Chr. Dis.*, 4: 267, Sept. 1956.
8. Gerard, M.: Genesis of Psychosomatic Symptoms in Infancy, in Deutsch, F.: The Psychosomatic Concept in Psychoanalysis. *Internat. Univ. Press*, New York, p. 82, 1953.
9. Gilbert, S. M.: Medical Aspects of Non-specific Ulcerative Colitis. *J. Med. Soc.*, N. J., 53: 443, Sept. 1956.
10. Groen, J., and Van der Valk, J. M.: Psychoso-

matic Aspects of Ulcerative Colitis. *Gastroenterologia,* 86: 591, 1956.
11. Lagercrantz, R.: Follow Up Investigation of Children with Ulcerative Colitis with Special Reference to Indications for Surgical Treatment. *Acta Paediatrica,* 44: 302, July 1955.
12. Lindemann, E.: Psychiatric Problems in Conservative Treatment of Ulcerative Colitis. *Arch. Neurol. and Psychiat.,* 53: 322, 1954.
13. Mohr, G. J., Josselyn, I. M., Spurlock, J., and Barren, S. H.: Studies in Ulcerative Colitis. Read at the 113th annual meeting of *American Psychiatric Association,* Chicago, Ill., May 13-17, 1957.
14. Paulley, J. W.: The Emotional Factors in Ulcerative Colitis. *Gastroenterologia,* 86: 709, 1956.
15. Prugh, D. G.: Childhood Experiences and Colonic Disorder. *Ann. New York Acad. Sc.,* 58: 355, 1954.
16. Richman, A., Sternlieb, I. Winkelstein, A.: ACTH and Cortisone Therapy in Ulcerative Colitis. *Am. J. Digestive Dis.,* 1: 206, Nov. 1956.
17. Sandweiss, D. J., and Sugarman, M. H.: What Is New in the Treatment of Ulcerative Colitis? *J. Mich. St. Med. Soc.,* 55: 1461, Dec. 1956.
18. Saver, G., Morris, R. R., Giansiracusa, J. E.: Psychotherapeutic Use of ACTH in Psychosomatic Disease. *Am. J. Psychiat.,* 112: 55, July 1955.
19. Sperling, M.: Psychoanalytic Study of Ulcerative Colitis in Children. *Psychoanalytic Quart.,* 15: 302, 1946.
20. Wirts, C. W., and Rehfuss, M. E.: Corticotropin in the Treatment of Ulcerative Colitis. *Gastroenterologia,* 86: 689, 1956.

Chlorpromazine in the Treatment of the Chronic Mental Patient in a Prison Hospital

(A Preliminary Report on 25 Cases With One Year Follow-up)

CHARLES E. SMITH, M.D., JAMES R. HARRIS, M.D.
and ALFRED L. GARRETT

The introduction of the tranquilizing drugs in the practice of institutional psychiatry has has been heralded with considerable enthusiasm and optimistic hopes that these drugs may relieve some of the intractable psychopathological dysfunction so frequently encountered in the chronic mental hospital patient. In general, early reports of clinical trials of these drugs indicated favorable results in the amelioration of some of the adverse symptomatology in the chronic patient. Stimulated by these reports, it was decided to employ chlorpromazine in a clinical trial on problem patients in a prison hospital.

The setting for this trial was the Medical Center for Federal Prisoners, Springfield, Missouri, a general medical hospital of 1,000 bed capacity with an average daily census of over 500 psychiatric cases of all types. The psychiatric service at this institution includes a staff of five psychiatrists, a psychologist, part-time nursing services, several social workers, an occupational therapist, medical technicians, and recreational aides. Somatic therapies including electroconvulsive therapy, coma and sub-coma insulin are available, as well as limited psychotherapy. In general, the psychiatric treatment program in this close-custody prison hospital is similar to that found in our better public mental institutions. The institution has the support of a sympathetic and enlightened penal administration which encourages the trial of all treatment techniques.

From the Psychiatric Service, Medical Center for Federal Prisoners, Springfield, Missouri.

Method

In selecting patients for trial on chlorpromazine in this project, it was decided to employ the most difficult management problems, which in this prison setting are the chronically hostile, aggressive, suspicious, often assaultive, paranoid psychotics. We proceeded with the idea that the over-all treatment program would be greatly enhanced if the drug proved of value in relieving these psychopathological syndromes.

Clinical Material:

A group of 25 male prisoners was selected for this study: 13 of these cases were white men, and the other 12 were colored. Their ages ranged from 20 to 48, with a mean age

of 32. In all but two cases, intelligence levels were average or better. The diagnostic categories are shown in Table I.

TABLE I

DIAGNOSTIC CATEGORIES

Diagnosis	*No. of Cases*
Schizophrenia, paranoid type	15
Schizophrenia, catatonic type	4
Schizophrenia, undifferentiated type	2
Paranoid personality	2
Psychotic depression	2

The duration of illness ranged from six months to 14 years, with the majority of cases being of at least several years' duration. Nine of these cases had received no prior somatic therapy. The others had all received courses of electroconvulsive or insulin coma therapy, or both; all without significant improvement.

Each of these individuals had a history of hostile, belligerent, threatening and assaultive behavior of considerable duration. Six had demonstrated self-destructive trends. For the most part, these men had been convicted of crimes against persons such as assault, murder, and rape (Table II).

TABLE II

TYPES OF OFFENSES

Offense	*No. of Cases*
Murder	4
Assault with intent of murder	3
Rape	4
Assault and robbery	7
Housebreaking	3
Mail theft	1
Mann Act	1
Car theft	1
Sodomy	1

Controls:

Having been impressed with the large number of possible overt physiological responses to the drug, which might serve to identify recipients, it was decided not to employ a control group on inert placebos. Instead, we elected to measure response to the drug by comparing behavior under its influence with well-established patterns which had been noted in these chronic patients prior to the administration of the drug. We are in agreement with the observation[1] that using the patient as his own control helps to eliminate subtle differences in handling from patient to patient, and gives a uniform baseline for comparison.

Precautions

In each case certain pre-treatment precautions were taken. These included a complete blood count, urinalysis, and serum bilirubin examination. During the course of treatment the serum bilirubin examination was repeated at weekly intervals.

Dosage Schedule and Duration of Treatment

With few exceptions these patients were uncooperative, so that it was necessary to give the initial dosage intramuscularly. Patients were started on 50 milligrams chlorpromazine intra-muscularly the first day, and if cooperative, the patient was given 50 milligrams twice a day orally on the second day. The following two days the patient was given 100 milligrams twice daily, and then the dosage was increased to 200 milligrams twice daily. By the end of a week most of the patients had reached a maximum dosage of 600 milligrams a day. A few of the cases were taken on to 1000 milligrams per day. All patients were continued on maximum dosage for a period of six weeks following which the medication was slowly reduced in the same manner in which it was started. There were no apparent withdrawal symptoms.

Technique of Administering the Drug

The administration of the drug presented special problems which are worthy of comment. This soon assumed the proportions of a full-time job, as it was often necessary to spend considerable time with the patient trying to gain his confidence, and persuade him to accept the medication. The needs for developing a special kind of patience, devotion and courage in this procedure made it apparent to us that success can well depend on the type of person who is selected to carry this out. In addition, the individual charged with this task inevitably develops meaningful personal relationships with the patient under treatment. Such relationships must be recognized as having some therapeutic value to the extent that they encourage socialization in these heretofore

hostile, withdrawn patients. The extent to which this factor contributed to the improvement of these patients is a matter which remains to be determined. There is, however, one disquieting observation to be made in this regard; namely, as acceptance of the drug grew, the technique of administration became more stereotyped, and it appeared that response to the drug diminished.

Evaluation Technique

For purposes of this study patients undergoing treatment were evaluated separately by three persons. The physician in charge of the project was responsible for making a pre-treatment evaluation of the patient, which covered a 12-month period preceding the onset of treatment. This survey included an enumeration of the number of times that a patient had been transferred from one ward to another because of his behavior, the number of aggressive acts and threats on record, the number of self-destructive attempts, a description of the regressive behavior he had shown, a notation of the duration of his illness, and a record of previous treatment and results. The work sheet included a diagnosis and a brief summary of the case.

In addition to completing the above material, the physician in charge of the projest was responsible for rating the patient at frequent intervals as to his reaction to treatment, the presence of hostility and paranoid trends, his sociability, cooperativeness, and any relevant observations on his personal habits and general behavior. Similar independent ratings of these same factors were made by the medical technician responsible for the administration of the drug, and a third set of observations was compiled by a selected group of trained ward personnel.

Results

A survey of these several independent ratings showed that during the course of treatment, improvement in some degree was observed in all but five cases. In most cases this improvement was classified as slight to moderate in degree. These improved patients were observed to sleep better, to be friendlier, and to show some reduction in their hostility and tension. Seven of these patients were improved sufficiently to permit their transfer to wards where they were allowed more freedom and received less supervision. However, in most instances, their stay on the improved ward was short-lived; that is, 7 to 10 days. Although behavior showed some seeming improvement in all cases, there were no cases in which the primary paranoid thought content showed any indication of alteration.

A re-evaluation of these cases at the termination of the 60-day period of treatment showed some degree of improvement in all but seven of these cases. For the most part the degree of improvement at this time was classified as slight, indicating that the patient was a little more manageable in the hospital.

One year after the termination of this treatment these cases were again re-evaluated. At this time it was found that only four of the cases were showing any improvement, with one described as making "a very good adjustment."

Complications

Several of the patients undergoing treatment complained of somnolence and dizziness. It was felt that this complaint may have occurred more frequently than was actually elicited from this group of somewhat withdrawn, inaccessible patients.

Noting a report[2] that obesity might be a serious complication in patients carried on moderate doses of chlorpromazine for lengthy periods of time, we examined the records of the weights of patients undergoing treatment. It was found that the average weight gain per patient during the 60-day period of treatment was 10.8 pounds. The largest amount gained by any one patient was 26 pounds and the smallest weight gain was two pounds. In general, patients undergoing treatment were observed to have improved appetite. However, we question whether the extensive weight gains noted can be accounted for completely by increased caloric intake. We feel that this finding is deserving of further study.

One of the cases developed an elevated serum bilirubin, with clinical evidence of jaundice, early in the course of treatment. The drug was discontinued and within a few

days the symptoms disappeared. Following this, the drug was resumed without any recurrence of this complication.

It was observed that in some cases patients responded to the drug initially by undergoing a period of excitement characterized by sudden explosive, assaultive behavior. Whether this reaction was due to the drug or to increased attention from the personnel, is a matter yet to be determined.

Summary and Conclusions

Of a group of 25 chronically disturbed, hostile, aggressive, paranoid patients in a maximum security prison hospital, 80% showed some degree of behavioral improvement during the early phases of a course of treatment with chlorpromazine. In most cases the degree of improvement was somewhat diminished by the end of the 60-day treatment period. A re-evaluation of these patients one year after cessation of treatment revealed that only four out of the 25 showed any improvement, and in only one of these cases was the improvement of a substantial nature.

As these patients began to show improvement, we saw a need for more trained personnel to work with them to increase their facilities and opportunities for socializing activities. We had a strong feeling that limitations in our staff may have prevented us from exploiting more fully the drug's potentiality for enhancing the patient's readiness for therapeutic participation in socializing activities.

We were impressed with the fact that the beneficial effect attributed to the drug seemed to diminish with the passage of time during the course of treatment. This observation leads us to raise several questions as follows:

1. To what extent can the beneficial results be attributed to increased attention to the patient and to suggestion?
2. Do these patients develop some tolerance to the drug which affects further improvement?
3. Do the results obtained justify continuing the dosage of the drug indefinitely?

We observed extensive weight gains in some of these patients, which could not be accounted for completely by increased caloric intake.

In the absence of more specific information on the long-range effects of this drug, we are faced with a serious decision as to how long its use should be continued with chronically-disturbed patients of the type in this study. We believe that more information is needed to answer these questions. In any event, we suggest that enthusiasm for the drug should not be allowed to blind us to the therapeutic value of socializing techniques.

Authors' Note: Chlorpromazine (Thorazine) was provided through the courtesy of the Smith, Kline & French Laboratories, Philadelphia, Pennsylvania.

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James R. Harris, Philadelphia General Hospital, Philadelphia 4, Pa.

Alfred L. Garrett, Medical Center for Federal Prisoners, Springfield, Missouri.

BIBLIOGRAPHY

1. Malitz, S., Hoch, P. H., and Lesse, S.: *Am. J. of Psychiat.*, 113: 540, Dec. 1956.
2. Lassenius, B., and Osterman, E.: *Nord. Med.*, 55: 798, 1956.

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2. "Remarks on ECT," Ugo Cerletti, M.D., Rome, Italy.

3. "Abnormal Cerebral Transmission and Psychosis," Amadeo Marazzi, M.D., Veterans Administration, Chief Research Lab. in Neuropsychiatry, Pittsburgh, Pa.

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